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Lowering Dietary Carbohydrates to Manage Obesity and Related Disease

A Systematic Review and Theoretical Framework

Dissertation submitted in accordance with the requirements of

University of Chester for the degree of Master of Science

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RADHIKA VERMA

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Abstract

Purpose: This study aimed to evaluate the lowering of carbohydrates from conventionally recommended levels of $\geq 55\%$ of energy intake as a valid and safe treatment option for managing obesity and related disease.

Methods: The study was a qualitative systematic review of fourteen randomized controlled studies, each with at least one study arm that lowered intake of carbohydrates to either ketogenic levels ($\leq 50\text{g/d}$) (Atkins type diet) or non-ketogenic levels including Zone type diets ($>50\text{g/d}$ to 40-45% of energy intake). Low-carbohydrate diets have generally implied increased protein intake to around 30% of energy intake. Outcomes evaluated included weight and fat loss; dyslipidemia; blood sugar control; hypertension; nutritional adequacy; hunger and satiety; adherence and safety. A synthesis of process, results and implications was used towards generating a theoretical weight management framework.

Results: In the short to medium term of up to six months both the ketogenic and non-ketogenic lowering of carbohydrates within the context of a calorie reduction of 300-750 kcal/day generated clinically meaningful weight loss results of 5-10%. Lower-carbohydrates diet plans generated similar or better results for most of the main outcomes examined as compared with conventional higher-carbohydrate/low-fat diet alternatives. Longer-term studies were few in number but weight loss results were in the range of 2-6% with no significant diet difference noted. Potential impact of ketogenic diets on dyslipidemia, renal and bone health needs further evaluation. When lowering carbohydrates or calories, nutritional adequacy may require management with the use of supplementation.

Conclusions & Implications: Lowering carbohydrates may provide an important and useful strategy to achieve a regular daily calorie deficit, generate clinically meaningful weight loss and improve related metabolic health markers. Recommended weight management protocols may be individualised based on a theoretical model that considers individual health risks and genetics, dietary preferences, carbohydrate sensitivity and is geared towards improved adherence.

Declaration

This work is original and has not been previously submitted in support of a Degree, qualification or other course.

Signed.....Radhika Verma.....

Date.....20 September 2012.....

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CHAPTER 1- INTRODUCTION

Obesity has been recognised by the World Health Organisation [WHO] as a world-wide epidemic and a major cause of various related metabolic disease co-morbidities including cardiovascular disease (CVD), type 2 diabetes (T2D), dyslipidemia, hypertension, osteoporosis and cancer (Despres, Lemieux & Prud'homme, 2001; James, 2008). Obesity has historically been an issue in affluent societies, in geographical areas and in periods of history where food is available in abundance to large sections of the population (Gordon, Goldberg & Chosy, 1963). Despite sustained efforts by individuals and governments, rates of obesity and overweight have remained on the increase. McMillan-Price & Brand-Miller (2004) noted that more than 40% of adults were overweight or obese in the United States (US), Europe and Australia. More recently, the United Kingdom (UK) Department of Health [DOH] (2012) has acknowledged that as per the last Health Survey for England, in 2010, 62.8% of adults and 30.3% of children were overweight or obese. Of these 26.1% of adults and 16% of children were obese.

Macronutrient intakes, namely carbohydrates, proteins and fats and their role in the optimal health as well as the management of obesity and related disease, have been the subject of interest over centuries (American Medical Association [AMA], 1974). The relative macronutrient composition of the diet in traditional hunter-gatherer societies (38% proteins, 39% fat, 23% carbohydrate) varied considerably with the macronutrient make-up of traditional western diets (16%

protein, 34% fat, 49% carbohydrate) (Cordain, 2002). Traditional diets have undergone significant changes with modernization. Higher-carbohydrate foods based on cereals, beans, dairy products and refined foods with sugar and cooking fat were not included in traditional diets (Bryngelsson & Asp, 2005). Some of these nutritional changes have been linked to resulting health problems particularly increased intake of saturated fat (Jew, AbuMweis & Jones, 2009) and the introduction of refined versions of sugar and flour (Westman et al., 2007). Western Government Health Authorities particularly in the US and the UK have since the 1960s and more emphatically since the 1980s, endorsed low-fat and higher carbohydrate eating plans to support cardiovascular health, optimal health and the management of obesity (Food Standards Agency [FSA] 2006; La Berge, 2008).

McMillan Price and Brand-Miller (2004) note that a low-fat / high-carbohydrate approach for obesity management is logical as carbohydrates have a relatively low energy density as compared with fat (4 kilocalories /gram (kcal/g) compared to 9 kcal/g for fat) thereby causing meals to be bulkier and more filling than high-fat meals. Pirozzo, Summerbell, Cameron and Glasziou (2003) further highlight that high-fat foods are relatively less satiating and favour both passive and active over-consumption due to improved taste and palatability. Cheuvront (2003) notes that the dietary macronutrient composition of 55% carbohydrates, 15% protein and 30% fat representing the current recommended protocol is supported by scientific research spanning twenty five years. However

challenges to the existing paradigm with differing macronutrient composition levels and/or caloric restriction have been made by several medical and nutrition professionals as well as lay people with personal experience by means of popular diet books (Skidmore, 2007). A small sample of low-carbohydrate bestsellers include 'The Carbohydrate Addict's Diet' (Heller & Heller, 1991), 'The Zone Diet' (Sears & Lawren, 1995), 'Dr. Atkins New Diet Revolution' (Atkins, 2002) and 'The South Beach Diet (Agatston, 2003)'. More recently The Dukan Diet (Dukan, 2010) first published in France in 2000 but republished in the UK in 2010 has gained popularity. Many of these approaches recommend a moderate to severe restriction of carbohydrate intake and are generally regarded and labelled as "Fad Diets" by the Medical Establishment (Saltzman, Thomason & Roberts, 2001). Nonetheless, some of these differing approaches are increasingly being included as the subject of scientific research and clinical trials (Dansinger, Gleason, Griffith, Lara-Castro & Garvey, 2004; Selker & Schaefer; 2005, Shai et al., 2008). The research is often initiated and funded by the Foundations promoting these so called "Fad Diets", to review and test popular belief and to arrive at clinical protocol in respect of diet and obesity management.

Pirozzo et al. (2003) highlighted that after more than two decades of the recommended low-fat /high-carbohydrate dietary approach, obesity and CVD has stood at much higher levels than in the 1980's. Astrup, Larsen and Harper (2004) noted that obesity has remained a significant worldwide issue despite a

substantial decrease in fat intake and pointed out that a compensatory increase in the intake of carbohydrates in the form of processed starchy foods and sugars was potentially responsible for this result. Gardner et al. (2007), following a study comparing low-carbohydrate diets with low-fat diets, support the idea that despite the higher levels of fat, particularly saturated fat, concerns about the adverse effects of low-carbohydrate diets on blood lipid and CVD risk are not substantiated.

Hite et al. (2010) highlight that US dietary guidelines to increase carbohydrates intake, reduce fat, saturated fat, salt, cholesterol were first proposed in 1977 and continue to be re-iterated (United States Department of Agriculture, [USDA], 2010). However the incidence of overweight, obesity and diabetes have increased. Hence potentially, the stigma attached to fat intake particularly saturated and polyunsaturated fats and the recommendation of higher carbohydrate intake based on the state of the science in the 1960s and 1970s may have to be re-evaluated in the light of more recent science (Hite, 2010; Taubes, 2011).

Three previous studies have performed systematic reviews on the efficacy and/or safety of low-carbohydrate diets however their conclusions are conflicting. Bravata et al. (2003) found that weight loss using low-carbohydrate diets was associated more clearly with decreased caloric intake and increased diet duration, not reduced carbohydrate content. Nordmann et al. (2006) and

Hession, Rolland, Kulkarni, Wise and Broom (2008) concluded that low-carbohydrate/high-protein diets were more effective than low-fat diets at reducing weight and cardiovascular risk at six months and were as effective if not more effective up to one year. Hence there remains a lack of clarity on the viability or effectiveness of low-carbohydrate diets for weight management purposes and the extent to which carbohydrates need to be lowered to promote effective weight management.

As a health advisor and nutritional therapist, this researcher is particularly interested in the potential to manage obesity and related CVD risk factors via dietary advice and protocol that can be sustained over time. Differences in views persist between UK and US government sponsored dietary advice in favour of a low-fat/higher-carbohydrate approach (FSA, 2006; USDA, 2010) and the increasing popularity of the low-carbohydrate approach to weight management being promoted by some medical doctors and health professionals with experience of treating obesity and related disease. Hence the rationale of this study is to assess the potential and validity of lower-carbohydrate diets and to consider a theoretical framework for the recommendation of restricting carbohydrate intake for the management of overweight, obesity and related disease.

CHAPTER 2 - LITERATURE REVIEW

Definition and Aetiology of Overweight & Obesity

Obesity is described as a condition where excessive fat accumulation in adipose tissue impairs health (DOH 2012; Goldberg, 2003). The UK DOH (1991, p. 52) Committee of Medical Aspects (COMA) of Food Policy in the UK confirmed that a body mass index (BMI) between 25 and 30 kilograms /meters squared (kg/m^2) may be described as overweight and above 30 kg/m^2 as obese. A BMI of 35 kg/m^2 or over is regarded as morbid obesity. This is in line with the WHO criteria for defining overweight and obesity (Allender & Rayner, 2007). The underlying reasons for and causes of obesity are complex and multifactorial and would include genetic susceptibility, reduced physical activity, consumption of excessive quantities of highly palatable, energy rich, easily available, energy dense food and other social and economic factors (Bouchard, 1991; McMillan-Price & Brand-Miller, 2004; Stein & Colditz, 2004).

Metabolic Disease Risk Factors of Obesity

Reaven (2005; 2006) describes insulin resistance as a defect in the ability of insulin to adequately perform the function of glucose disposal and is potentially responsible for a cluster of cardiovascular risk factors associated with obesity termed as metabolic syndrome (Fonseca, 2005; Reaven, 2006). The defining components of metabolic syndrome are three or more of the following criteria: central obesity as evident from an elevated waist circumference, elevated triglycerides (TAG), reduced high-density lipoprotein cholesterol (HDL-C),

elevated blood pressure and elevated fasting blood glucose (Fonseca, 2005; Reaven, 2006). Lara-Castro & Garvey (2004) concur that insulin resistance is the key issue underlying the pathogenesis of metabolic syndrome and is associated with generalized obesity and the accumulation of body fat. Despres et al., (2001) highlight that abdominal obesity, particularly visceral adipose tissue has been associated with glucose intolerance and hyperinsulinaemia resulting from insulin resistance and results in increased risk of CVD (Fonseca, 2005). Heller and Heller (1994) draw a significant link between chronic elevated circulating insulin, as seen in obese subjects, to atherosclerosis, hypertension, non-insulin dependent diabetes mellitus (NIDDM), CVD and some forms of cancer and stroke.

Reaven (2005) suggests that low-fat/high carbohydrate diets do not rectify the basic defect of insulin resistance rather they increase the metabolic manifestations. Reaven (2005) further reiterated that the practice, since the 1960's, of replacing saturated fats by carbohydrates is not supported by the available research. Reaven (2005) proposes that the treatment of insulin resistance requires weight loss and making dietary macronutrient changes that replace saturated fat with unsaturated fats and not with carbohydrates. There is widespread belief and sufficient evidence that weight loss, even as low as 5-10% favourably affects markers of metabolic disease (Despres et al., 2001; Lara-Castro & Garvey, 2004) and can improve insulin sensitivity (Reaven, 2005). Hence pursuing weight loss of 5-10% is regarded as clinically meaningful

to the improvement of metabolic health and the reduction of carbohydrates in the diet has a potential significance for managing insulin resistance.

Historical Context to Carbohydrate Restricted Diets for Weight Loss

The first available account of a successful restricted-carbohydrate weight loss diet for an individual was by Banting (1869) which called for restriction of sweet and starchy foods to support weight loss while allowing *ad libitum* meat intake (Banting, 1869; American Medical Association [AMA], 1974). Pennington (1953a; 1953b) set out an alternate approach to the problem of obesity using a low-carbohydrate calorically unrestricted diet (AMA, 1974). Gordon et al. (1963) undertook a clinical trial and demonstrated successful weight loss with calories restricted to 1320 calories and ratios from protein: fat: carbohydrates of 30:55:15 but with an emphasis on unsaturated fats.

The very low-carbohydrate diet in 'Dr Atkins Diet Revolution, 1972' (as cited by AMA, 1974) was heavily criticised by the AMA (1974) with concerns over levels of saturated fats and cholesterol rich foods permitted. Atkins (2002) published a revised edition of the 'Atkins Diet Revolution', re-iterating recommendations of restricting carbohydrate intake to $\leq 20\text{g}$ for two weeks followed by an increase of 5g per day for each week following up to a maximum of 50g of carbohydrate intake per day.

Other medical and nutrition professionals have developed alternative versions of the low-carbohydrate/high-protein diet claiming to address some of the shortfalls of the Atkins Diet (Kauffman, 2004). The Zone Diet (Sears & Lawren, 1995) recommended lowering carbohydrate intake from the conventional diet levels of $\geq 55\%$ to 40% of energy intake with 30% of energy emanating from dietary proteins and fats respectively. Hence lowering carbohydrates to manage obesity has a history that spans more than a century and potentially warrants closer consideration.

Defining Low-Carbohydrate Diets

There is no clear definition of a low-carbohydrate diet and diets that limit carbohydrate have been variously described as “low-carbohydrate”, “very-low-carbohydrate”, “high-protein”, “high-fat” and “ketogenic” (Westman, Mavropoulos, Yancy & Volek, 2003). Adam-Perrot, Clifton and Brouns (2006) suggest low-carbohydrate refers to less than 100g of carbohydrates per day. Boucher, Benson, Kovarik, Solem and VanWormer (2008) refer to low-carbohydrate as $<130\text{g/day}$. Westman et al. (2007) note that diets with a carbohydrate intake of $<20\text{-}50\text{g/d}$ are referred to as low-carbohydrate ketogenic (LCK) diets whilst carbohydrate intakes of $50\text{-}150\text{g/d}$ are unlikely to generate ketone bodies and could be referred to as low-carbohydrate non-ketogenic diets (LCNK). Additionally a nutritional intake of $<200\text{g}$ of carbohydrate is sometimes called a low-carbohydrate diet but may not generate the associated and expected metabolic changes. (Westman et al., 2007).

Potential Mechanisms for the Effectiveness of Low-carbohydrate Diets

Johnstone, Horgan, Murisin, Bremner and Lobley (2008), note that when carbohydrate intakes are very low (< 20 g /d), the reduced glucose availability causes a ketogenic state to occur and a generation of ketone bodies from fat reserves. Westman et al. (2003) suggest that when carbohydrates are severely restricted, energy is derived from ketones and fatty acids in place of glucose. Whilst a ketogenic state is not essential for improved satiety, less hunger and reduced caloric intake result. Additionally, voluntary intake of energy appears to be less when carbohydrate intake is <10% of energy as compared with higher levels of carbohydrate intake of 35-45% of energy intake (Johnstone et al., 2008). Bryngelsson and Asp (2005) highlight that carbohydrates are a preferred source of energy and that fat burning is suppressed when glucose is available. Hence carbohydrates and sugars are regarded as fattening and excess carbohydrates encourage *de novo* lipogenesis (Bryngelsson & Asp, 2005).

Leidy, Mattes and Cambell (2007) show that during weight loss, protein intake influences appetite, the hunger stimulating hormone – ‘ghrelin’ and thermogenesis. Astrup et al. (2004) summarise some of the recognised mechanisms that may account for weight loss related to a low-carbohydrate diet. These include increased excretion of bound water caused by depletion of carbohydrate stores; the appetite suppressing effects of a ketogenic diet; the greater satiating effects of and the reduction in spontaneous food intake associated with the implied higher protein levels associated with a low-

carbohydrate diet; a reduced energy intake due to limited food choices (Astrup et al., 2004; Bryngelsson & Asp, 2005).

Davis et al. (2009) concur that carbohydrates are the primary source of glucose for metabolism and that reducing carbohydrate intake can reduce insulin levels, improve glycemic control, improve insulin sensitivity and reduce postprandial hyperglycemia. Heller and Heller (1994) promote a theory that frequent daily intake of carbohydrates sustains chronic hyperinsulinemia and insulin resistance and reducing the frequency of carbohydrate intake is required to manage these conditions without necessarily reducing the recommended 55-60% of daily energy intake from carbohydrates.

McMillan-Price and Brand-Miller (2004) have highlighted the high-glycemic effect of many of the carbohydrates included in a typical western diet including potatoes, breads, and low-fat cereal products. The intake of these foods result in a high-glycemic load and increased demand for insulin often causing the chronic hyperinsulinemia referred to above by Heller and Heller (1994). Hence there are apparent mechanisms that support the theory that a restriction of carbohydrate intake and/or the alteration of the quality of or frequency of carbohydrates intake may impact on insulin resistance, hunger indicators, satiety, appetite control and consequently body weight and obesity management.

Toxic Environment

Horgen and Brownell, 2004 note that the root of the obesity epidemic crisis may be related to the 'toxic environment' which surrounds people with inexpensive, heavily marketed, convenient foods high in fat and calories and promotes reduced physical activity. Schwartz and Brownell (2007) suggest that the key drivers of human over-consumption are flavour variety, large portions, visibility and proximity. Many of the un-healthy foods readily available contain refined and processed carbohydrates and sugars or high-fat fried foods. Hence lowering carbohydrates could aim to reduce consumption of junk and/or processed foods and sugars and consequently impact positively on obesity management.

Psychological & Behavioural Factors

Brownell and Wadden (1992) highlight that behaviour is significant both in the aetiology and treatment of obesity and that long-term weight-management ultimately depends on the ability of patients to alter their behaviour patterns with respect to diet and exercise. Self-monitoring, stimulus control, cognitive restructuring and reinforcement by reward are behavioural treatment techniques that have been researched and remain important tools to improve the success of weight management protocols in clinical and domestic settings (Brownell & Stunkard, 1978). Bond, Phelan, Leahey, O'Hill and Wing (2009) highlight the significance of the loss of control over eating ('disinhibition') and the degree of conscious control over eating ('cognitive restraint') as behaviours significant to

weight management. Davis and Turner (2001) re-iterate that weight maintenance requires life-long behavioural changes combining exercise with dietary changes and social support.

Patel and Hu (2008) suggest that short sleep duration appears to be independently associated with weight gain due to increased caloric intake and reduced energy expenditure that may potentially result from sleep deprivation. Spiegel et al. (2004) note that sleep plays a significant role in energy homeostasis and that the satiety hormone 'leptin' levels are dependent on sleep duration. Healy and Schwartz (2010) highlight that chronic stress can lead to truncal obesity and insulin resistance. Hence in addition to dietary issues, consideration of psychological and behavioural influences on weight management are potentially relevant.

CHAPTER 3 - METHODOLOGY

Research Questions

The key research questions being raised are if and how obesity, abdominal obesity and related co-morbidities may be influenced by diet and macronutrient composition. In particular, can obesity and related health markers be managed via lowering carbohydrate intake which usually implies increased protein intake? Are lower-carbohydrate diets beneficial for weight management both in absolute terms and in comparison to the more widely accepted conventional higher-carbohydrate/low-fat or other low-calorie dietary approaches? Are low-carbohydrate diets safe and effective and may they be recommended in clinical practice? Furthermore if the lay press and some potentially informed medical professionals recommend lowering carbohydrates for obesity management via popular literature, why are these not generally prescribed by health authorities?

Study Design

The study design is that of a systematic review which aims to identify and provide an overview of all relevant literature on the given topic and is also referred to as a “systematic literature review” (Green, 2005). Cook, Mulrow and Haynes (1997) discuss systematic reviews as being a process that synthesizes best evidence for clinical decisions. Like other types of research, systematic reviews are subject to bias, which requires management via rigorous methods and reproducible criteria to be included in the review (Cook et al., 1997). In contrast to the three other systematic reviews on the subject of low-

carbohydrate diets (Bravata et al., 2003; Hession et al., 2008; Nordmann et al., 2006), and to enable better focus on the theoretical issues, the results of the underlying studies have not been statistically combined. Accordingly this study may be regarded as a qualitative systematic review (Cook et al., 1997; Jadad, 1998, p. 83). In addition the study may be regarded as an evaluation as it uses scientific method and systematic collection of data to assess the effectiveness of interventions (Bowling, 2002, p.9) and involved exploring how existing knowledge may be used to inform and guide practical clinical guidelines (Jadad, 1998, pp. 90-91).

Data Searches

Several searches were performed on the PubMed database using search strings such as “weight loss AND carbohydrate”; “diet AND obesity AND cardiovascular”, “proteins AND low carbohydrate AND weight”, “high protein AND weight loss”, “weight loss AND macronutrient”. The search strategy aimed to identify studies between 2000 and 2010; was limited to studies in English; and to the search terms “clinical trial”, and “randomized controlled trial”; with subjects that were adult of 19+ years. Titles and abstracts were reviewed to identify relevant studies and in addition reference lists of selected studies were scrutinised to identify additional studies that might be relevant. However the final selection was limited to studies for which full text articles were available. In addition a wide range of popular diet books relating to lowering carbohydrate

intake towards the management of obesity and related disease were reviewed for relevant concepts, empirical experience and supporting research articles.

Study Selection Criteria

The available studies were diverse in design. The intention was to include randomized controlled trials (RCTs) regarded as “the gold standard” in terms of quality of evidence (Hart, 2003). Hence, most of the study designs considered and/or selected had participants randomized to receive one or more low to moderate carbohydrate diets compared with alternative diets that were generally low-fat or low-calorie in content. All studies that involved lowering carbohydrate intake as part of the study design were considered for inclusion irrespective of the title of the study or description of the diet. Specifically, studies that referred to high-protein (HP) diets were considered for inclusion if the HP diet design implied a low carbohydrate diet content. Only studies conducted in an outpatient setting were included to represent the researcher’s interest in a clinical setting. Target end-points or clinical end-points were identified and studies were excluded if they did not report data for at least one of the obesity body composition outcomes and one of the co-morbidity related clinical outcomes and in particular dyslipidemia markers. Fourteen studies were finally selected for inclusion in the review.

Data Collection

The data collection codes and categories were obesity represented by weight, body mass index (BMI) and body fat measures including abdominal obesity represented by waist circumference (WC). In addition relevant metabolic disease and CVD related end points considered were blood glucose, insulin resistance and/or insulin sensitivity; dyslipidemia indicators including total cholesterol (TC); triglycerides (TAG), high density lipoprotein cholesterol (HDL-C) and low density lipoprotein cholesterol (LDL-C) particularly LDL-C particle size (Despres et al., 2001); and hypertension indicators. Other information collected included hunger and satiety indicators, dietary adherence, adverse effects, exercise and activity levels and supervision and monitoring undertaken.

Data Evaluation

The selected trials were evaluated against a series of criteria based on selected references as listed in Appendix A1. The criteria were expanded to develop a research analysis tool and instrument for data collection (Kumar 1999, p. 125) that would cover the key elements of dietary studies for the purpose of management of obesity and related disease. The criteria aimed to evaluate the relevance of the study, the methodology, results and their interpretation to the research question being considered. In addition the criteria aimed to assess the external validity of the studies to the researcher as a nutritional therapist in ascertaining a sustainable protocol for overweight and obesity and related co-morbidities in clinical practice.

Results from the application of the research tool for each of the fourteen studies included in the review are attached as appendices A2-A15. The complexity of the dietary studies in terms of the number of variables and variety of measurement methodologies adopted made analysing each of the studies to address the questions raised by the research tool excessively time consuming. Hence as a time-saving method, the research enquiry tools were completed where relevant, with direct extracts from the papers and broadly referenced as such in the Appendices A2 to A15. The length and detail included in the research tool was designed to provide adequate original comment from the studies to enable the synthesized conclusions to be corroborated in any subsequent review.

The data collection sheets (Appendices A2-A15) highlight the various influences on the outcomes of a typical weight loss study namely duration, caloric restriction, macronutrient composition, saturated and other fat levels, fibre levels, activity and exercise levels, supervision and monitoring. Tables 1, 2 and 3 with a related key for abbreviations and Appendix B1 derived from the data collection sheets summarise the diversity of dietary design and protocol for the low and moderate carbohydrate diets included in this review and the comparative diets.

CHAPTER 4 - RESULTS

Identified Studies & Study Characteristics

Based on the search on Pubmed, fourteen studies were identified to be included in the review. The dietary studies selected included a range of diets with differing recommended macronutrient ratios particularly manipulating carbohydrate levels as described in Appendix B1 and shown in Tables 1, 2 and 3. The low and moderate carbohydrate studies were collated within two main categories. Low-carbohydrate ketogenic (LCK) Atkins type diets (Table 1) and low-carbohydrate non-ketogenic (LCNK) diets including the moderate carbohydrate Zone type diets which are also non-ketogenic but recommend a diet protocol of carbohydrates: protein: fat of 40:30:30 (Table 2). Sacks et al. (2008) included two diets which had 40% fat and either 35% or 45% of energy from carbohydrate with the balance of 25% and 15% respectively from protein intake. Both these diets were regarded as a closer to the Zone type diets and have been categorised as such.

In total the review considered twelve Atkins type diets (Table 1), fifteen low-carbohydrate non-ketogenic diets (Table 2), of which twelve were moderate-carbohydrate Zone type diets (Table 2), giving data on twenty seven low to moderate carbohydrate interventions. These were assessed against twenty low-fat diets (Table3) with a fat intake ranging from 10-30% and carbohydrate intake generally higher than 55% and 2 low-calorie dietary interventions. Hence this review permits a study of low and moderate carbohydrate diets, makes a

comparison between ketogenic and non-ketogenic low-carbohydrate diets and enables both low and moderate carbohydrate diets to be assessed against the generally recommended low-fat/higher-carbohydrate conventional diets.

Table 1. Low-Carbohydrate Ketogenic Diets (LCK) / Atkins Diets (A) (Alphabetical Order)						
Study Study Arms	Year	Duration	Protein %	Carbohydrate %	Fat %	Calories (kcal) / Diet Detail
Dansinger : A A:Z:L:W	2005	1 yr /52w	NS	< 20g increased up to 50g per day	NS	NCR. MCR=138 1921 kcal p/d actual
Foster: A A:L	2003	3m/13 w 6m/26 w 1 yr /52w	NS	Atkins diet rules	NS	NCR
Johnston: A A:Z	2006	6 w	30%	5% increased by 5g p/w in weeks 3-6 to between 20g – 40g /day	60% SF-30%	1500 kcal isocaloric
McAuley :A A:Z:L	2004	8 w ; 16w & 24w	NS-	20g p/d for 2 weeks. 5g increase per week till 50g of C by week 8	NS	NCR required. Resulting deficit in kcal- 519 kcal (8w); 384 (16w) ; 381 (24w)
Samaha :A A:L	2003	6 m /26w	NS	<30g per day	NS	NCR
Shai : A A:L:M	2008	2 yr / 104w	NS	<20g of C per day for 2months gradual increase to 120g p/d.	NS	NCR
Stern :A A:L	2004	1 yr / 52 w	NS	<30g per day	NS	NCR
Yancy : A A:L	2004	24m / 104 w	NS	5g per day raised weekly AC=29±11.1g – 8% of daily intake	NS	NCR required Average intake for Atkins group 1461 kcal
<p>KEY : A=Atkins ; AC=actual consumption; C= carbohydrates; g=grams; kcal= kilocalories; L=low fat/high carbohydrate; LCK=low carbohydrate ketogenic; m=months; M= Mediterranean diet; MCR= Mean Caloric Restriction; NCR= No calorie restriction; NS = not specified; p/d= per day; p/w=per week; SF= saturated fat; w =weeks; W= Weight Watchers; yr = year; Z=Zone.</p>						

Table 2- Low-Carbohydrate Nonketogenic Diets (N) Including Zone (Z) Type Diets							
Lower Carbohydrate Non Ketogenic diets (N) – >50-120g /d of carbohydrate							
Study Study Arms	Year	Duration	Protein %	Carbohydrate %	Fat %		Calories (kcal)/Diet Detail
Luscombe- Marsh LF/HP N:N	2005	12 w	40%	30% (110g/d) Fibre :21g/d	30% SF≤10 %		ER: 1500kcal (30%) ER 1434 kcal, C=30%
Luscombe- Marsh HF/SP N:N	2005	12 w	20%	30% (110g/d) Fibre 27g /d	50%		ER: 1500kcal (30%) 1434 kcal C=30%
Meckling N N:L	2004	10 w	-	Reducing C from 100g to 50- 70g by day 5 Achieved reduction 228 g/d	-		Wm:1205-1605 kcal Mn: 1402-2200 kcal Deficit: 763 kcal (33%)
Lower/Moderate Carbohydrate Zone type diets (Z) - Protein (30%)/Carbohydrate (40%)/ Fat (30%)							
Study Study Arms	Year	Duration	Protein %	Carbohydrate %	Fat %		Calories (kcal)/Diet Detail
Dansinger Z A:Z:L:W	2005	1 year	30%	40%	30%		NCR; MCR=251 1808 kcal/d actual
Frisch Z Z:L	2009	6m & 1yr	25%	<40%	>35%		Required deficit :500 kcal Actual ER : 400 kcal
Johnston Z A :Z	2006	6 w	30%	40%	30% - SF 30%		1500kcal isocaloric
Layman Z(HP) Layman Z+EX (HP) Z:Z+EX:L	2005	16 w	30% 1.6g/kg /day Actual: 107g/d	40% C:P Ratio<1.5 AC: C:P = 1.24 (30%) fibre of 17g	30% 57g of fat Actual 32%		1700 isocaloric diets
McAuley Z (HP) A:Z:L	2004	8 w; 16w & 24w	30%	40%	30% (mainly MUFA)		5 meals < 5hrs apart NCR required; Resulting deficit of kcal- 522(8w); 346(16w); 403(24w)
Parker Z Z:L	2002	8 w ER 4w EB	28%	42%	28% SF-8%, MUFA- 12% PUFA – 5%		ER =1600
Sacks Z (HF) Z:Z:L:L	2008	24 m	25% 15%	35% 45% Fibre: 20g	40% 40% SF≤8%		750 kcal deficit
KEY : A=Atkins ; AC=actual consumption; C= carbohydrates; EB= Energy Balance; ER= energy restriction; EX= Exercise; g=grams; g/d=grams per day; g/kg/d= grams per kilogram per day; HF= high fat; hrs= hours; HP= high protein; kcal= kilocalories; L=low fat/high carbohydrate; LF= lower fat; m=months; MCR= Mean Caloric Restriction; Mn=men; MUFA=monounsaturated fatty acids; N= low-carbohydrate non-ketogenic; NCR= No calorie restriction; P=Protein; PUFA= polyunsaturated fatty acids; SF= saturated fat; SP= standard protein; w =weeks; W= Weight Watchers; Wm= women; Yr=year; Z=Zone.							

Table 3: Comparative Diets Included In Study - Low-Fat/Higher Carbohydrate (L); Low-Fat – Ornish Diet (O); Low-Calorie (LCAL)-Mediterranean Diet (M), Weight Watchers Diet (W)							
Low-Fat / Higher Carbohydrate Conventional Diets (L)							
Study Study Arms	Year	Duration	Protein %	Carbohydrate %	Fat %		Calories (kcal)/Diet Detail
Dansinger (L):O A:Z:L:W	2005	1 yr / 52w	NS	NS	10%		MCR=192
Foster L A:L	2003	1 yr/52w	15%	60%	25%		Wm: 12-1500 Mn: 1500-1800
Frisch L Z:L	2009	6m / 26 w & 1yr /52 w	15%	55%	<30%		RD= 500 kcal ; AD= 400 kcal deficit for 6m; Below baseline at 12m
Layman L Z:Z+EX: L:L+EX	2004	16 w	15%; 0.8g/ kg/d AC:18 %	52.5-55%. Fibre 17g C:P >3.5 AC: 198g/d (61%)	30%. 57 g of fat AC: 25.5%		1700 isocaloric diets Free-living Actual: 1300-1400kcal (ER=33%)
McAuley L A:Z:L	2004	8w, 16w; 24w	15%	>55%	<30%		NCR required; Resulting deficit of kcal- 439 (8w); 343 (16w); 350 (24w)
Meckling L N:L	2004	10 w	NS	AC=Increase of 13g/d from start level of 100g/d.	NS		Wm:1205-1605kcal M : 1402-2200 Deficit: 607 kcal (29%)
Parker L(LP) Z:L	2002	8 w	16%	55%	26% SF-8%, MUFA-12% PUFA – 5%		ER-1600kcal
Sacks L (HC) Z:Z:L:L	2008	24 m / 104 w	15% 20%	Fibre:20g 65% 55%	SF≤8% 20% 20%		750 kcal deficit
Shai – L A:L:M	2008	2 yr/ 104w	NS	NS	30%		W: 1500 kcal M: 1800
Samaha L A:L	2003	6m/26w	NS	NS	≤30%		500 kcal deficit
Stern L A:L	2004	1 yr/ 52w	NS	NS	≤30%		500 kcal deficit
Yancy L A:L	2004	24 w	AC= 197.6± 34.2g – 52% of daily intake	NS	<30%		500-1000 kcal reduction. Average energy intake 1502 kcal
Other Low Calorie Diets (LCAL)							
Dansinger W A:Z:L:W	2005	1 yr / 52w	NS	NS	NS		ER: 1200-1600 kcal MCR=244
Shai – M A:M:L	2008	2 yr / 104 w	NS	NS	NS		W: 1500 kcal M: 1800 kcal
KEY : A=Atkins ; AC=actual consumption; AD= actual deficit; C= carbohydrates; EB= Energy Balance; ER= energy restriction; EX= Exercise; g=grams; g/kg/d= grams per kilogram per day; g/d= grams per day; HC= high carbohydrate; kcal= kilocalories; L=low fat/high carbohydrate; LCAL= low-calorie diet m=months; LP= low protein; M= Mediterranean diet; MCR= Mean Caloric Restriction; Mn=men; MUFA=monounsaturated fatty acids; N= low-carbohydrate non-ketogenic; NCR= No calorie restriction; NS= not specified; P=Protein; PUFA= polyunsaturated fatty acids; RD=required deficit; SF= saturated fat; w =weeks; W= Weight Watchers; Wm= women; yr= year; Z=Zone.							

The results of the individual studies can be synthesised under some broad headings. The primary outcomes identified by this study are the effects of carbohydrate restriction on weight loss both in the short term of up to six months; weight loss over the longer term of twelve to twenty four months; and fat loss and/or waist circumference results. Furthermore, the mechanisms underlying and influences on weight loss and fat loss potentially as a result of carbohydrate restriction are assessed including energy restriction; impact of protein intake; cultural and gender effects and the effects of exercise. Additionally the impact of carbohydrate restriction is considered in relation to lipid control; insulin and glycemic control; hypertension; hunger and satiety indicators; attrition and adherence to dietary protocol; quality of nutrient intake and nutritional adequacy; and safety and side effects. The results from the selected studies are expressed both in absolute terms and in relation to low-fat higher carbohydrate alternatives where relevant.

Weight Management Results

Where data was available, reported mean weight loss and percentage mean weight loss from baseline was tabulated by reference to intervention duration of the weight loss phase of the study and information on caloric restriction (prescribed or resulting) to permit analysis of the impact of both duration and caloric restriction on weight loss results (Tables 4, 5 & 6; Appendices B1 & B2). Figure 1 shows the mean weight loss and percentage of mean weight loss from

baseline results for the low and moderate carbohydrate diets included and summarised in Appendix B1 and Tables 4 and 6.

Table 4 : Low and Moderate Carbohydrate Interventions (Up to 6 months Duration) - Mean & Percentage Weight Loss and Mean Energy Deficit / Day			
Study / Duration	Mean Weight loss in kg	% Weight Loss	Mean Energy Deficit /day (E=estimated deficit from 2000 kcal)
Atkins Type Diet			
Foster et al. (2003) 3 months 6 months	6.7 kg 6.9 kg	6.8% at 13 w 7.0% at 26 w	No calorie restriction (NCR) but reduced calories consumed
Johnston et al. (2006) 6 weeks	6.3 kg	6.6% at 6 w	500 kcal (E)
McAuley et al. (2004) 8 weeks 16 weeks 24 weeks	6.6 kg 6.9 kg 7.1 kg	6.9% at 8 w 7.1% at 16 w 7.3% at 24 w	519 kcal 384 kcal 381 kcal
Samaha et al. (2003) 6 months	5.8 kg	4.4% at 26 w	NCR but less than low-fat (LF) comparative
Yancy et al. (2004) 24 weeks	12.0 kg	12.9% at 24 w	1461±325 kcal. – Deficit 500 (E)
Non-Ketogenic low-carbohydrate Diets			
Luscombe-Marsh et al. (2005) N (HF/SP) N (LF/HP)	10.2 kg 9.2 kg	10.2% 9.5%	500 (E) kcal
Meckling et al. (2004) 10 weeks	7.0 kg	7.6% at 10 w	400-800 (E) kcal
Non-Ketogenic low-carbohydrate Zone Type Diets			
Frisch et al. (2009) 6 months	7.2 kg	7.1% at 26 w	400 kcal
Johnston et al. (2006) 6 weeks	7.2 kg	7.2% at 6 w	500 (E)
Layman et al. (2004) – 16 weeks Z Z+EX Average (Z & Z+EX)	8.7 kg 9.8 kg 9.3 kg	9.5% at 16 w 11.3% at 16 w	300 (E) -1700 kcal/day
McAuley et al. (2004) 8 weeks 16 weeks 24 weeks	5.4 kg 7.0 kg 6.9 kg	5.8% at 8 w 7.3% at 16 w 7.4% at 24 w	522 kcal 346 kcal 403 kcal
Parker et al. (2002) – 8 weeks	4.5kg	4.6 % at 8 w	400 (E) – 1600 kcal/d
Sacks et al. (2008) 6 months	6.0 kg	6.5 % at 26 w	750 kcal

As the studies included were RCTs, the control groups were assigned alternative diets which in the main were higher-carbohydrate/low-fat, conventional diets (Tables 5 & 6) representing the existing paradigm and the diet that most health government health authorities in the UK and the US continue to support. Figure 2 shows the relative mean percentage weight loss for the various diet arms included in each study to permit a comparative analysis. Both figures 1 and 2 are shown in order of intervention duration to assess trends related to the length of the intervention on weight loss achieved.

Table 5 : Low-Fat/High Carbohydrate Interventions (Up to 6 Months Duration) - Mean & Percentage Weight Loss and Mean Energy Deficit /Day			
Study /Duration	Mean Weight loss in kg	% Weight Loss	Mean Energy Deficit /day (E=estimated) in kcal/day
Low- Fat Diets (L)			
Foster et al. (2003) 3 months 6 months	2.6 kg 3.1 kg	2.7 % at 13 w 3.2 % at 26 w	Women (Wm):(E) 650 kcal/d; Men (Mn) : (E) 350 kcal/d
Frisch et al. (2009) 6 months	6.2 kg	6.3 % at 26 w	400 kcal /d
Layman et al. (2004) L L + Exercise (EX)	7.8 kg 6.7 kg	8.3 % at 16 w 8.4% at 16 w	300 (E) -1700 kcal/d
McAuley et al. (2004) 8 weeks 16 weeks 24 weeks	4.3 kg 4.4 kg 4.7 kg	4.4 % at 8 w 4.5 % at 16 w 4.8 % at 24 w	439 kcal/d 343kcal/d 350kcal/d
Meckling et al. (2004) 10 weeks	6.8 kg	7.4% at 10 w	607 kcal (29%)
Parker et al. (2002) 8 weeks	4.5 kg	4.9 % at 8 w	400 kcal/d (E)
Sacks et al. (2008) 6 months	6.0kg	6.5% at 26 w	750 kcal kcal/d
Samaha et al. (2003) 6 months	1.9 kg	1.4% at 26 w	500 kcal /d
Yancy et al. (2004) 24 weeks	6.5 kg	6.7 % at 24 w	500-1000 kcal /d reduction expected. Average intake 1502 kcal 500 kcal/day (E)

Weight Loss Achieved (Up to Six Months) – Absolute and Percentage

For interventions spanning 6 weeks to 6 months with varying levels of caloric restriction of 300 to 750 kcal per day as shown in Table 4, most of the carbohydrate restricted diets included showed a mean weight loss of between 5 and 10 kilograms of body weight from baseline as shown in Table 4 and Figure 1. Percentage weight loss from baseline mirrored mean weight loss as shown in Figure 1 and similarly was between 5 and 10% for most of the low and moderate carbohydrate interventions that extended up to six months. These included Atkins type diets, non-ketogenic low-carbohydrate diets and Zone type diets. The similarity between weight loss in kilograms and percentage weight loss may be explained as baseline weight was generally in the region of 90-100kg.

A few exceptions were noted where weight loss was outside the range noted above. In Parker, Noakes, Luscombe and Clifton (2002), the Zone type intervention generated a mean weight loss of 4.6% at eight weeks with a calorie intake restricted to 1600 kcal. The percentage weight loss was marginally lower than the results for the other Zone type diets included in this review though after an additional four weeks of energy balance the weight loss percentage for the zone diet group was 5.3% suggesting an independent effect of diet composition.

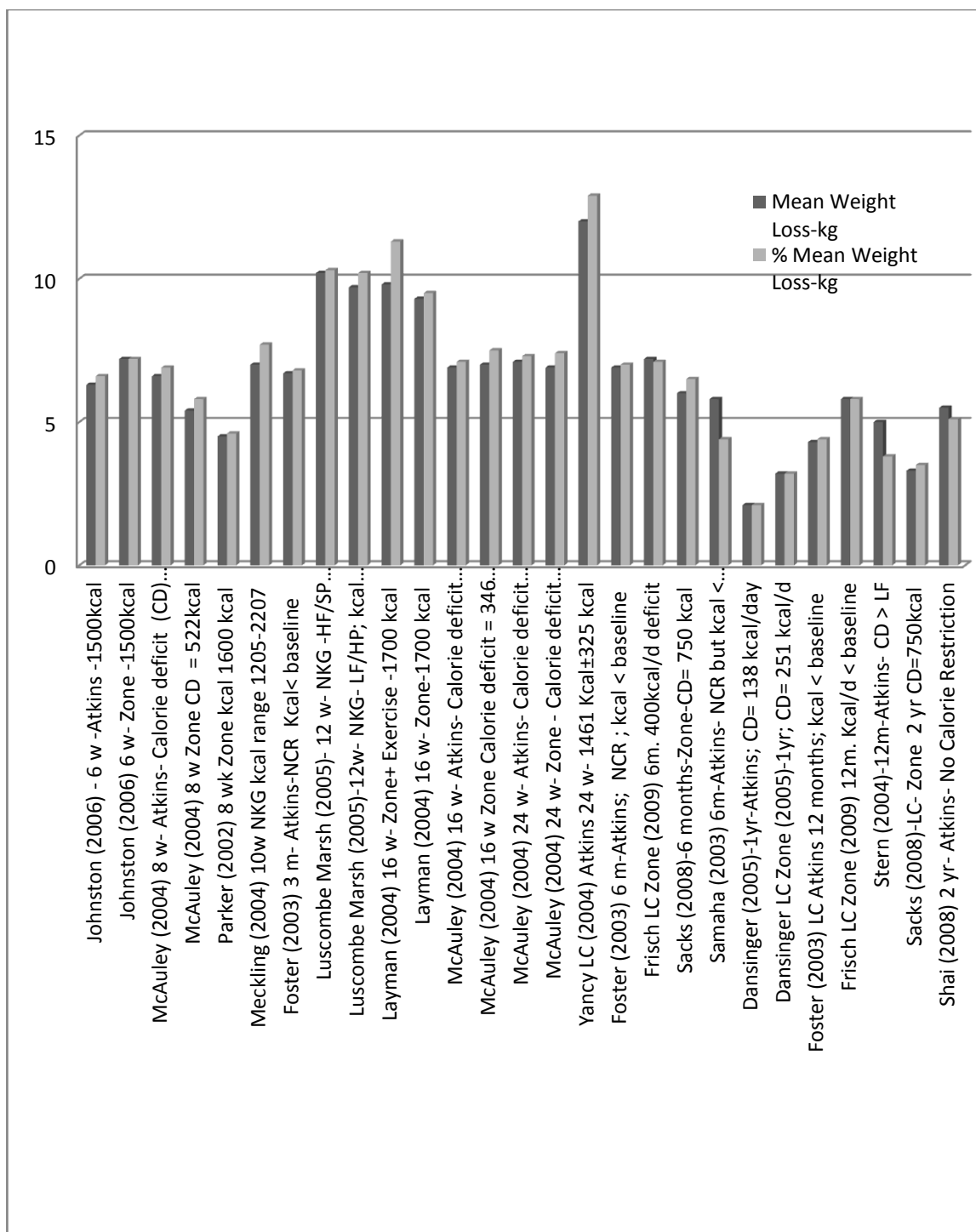


Figure 1: Mean Weight Loss in Kilograms (kg) and Percentage of Mean Weight Loss From Baseline For Low And Moderate Carbohydrate Diets Included In the Study – In Order of Intervention Duration.

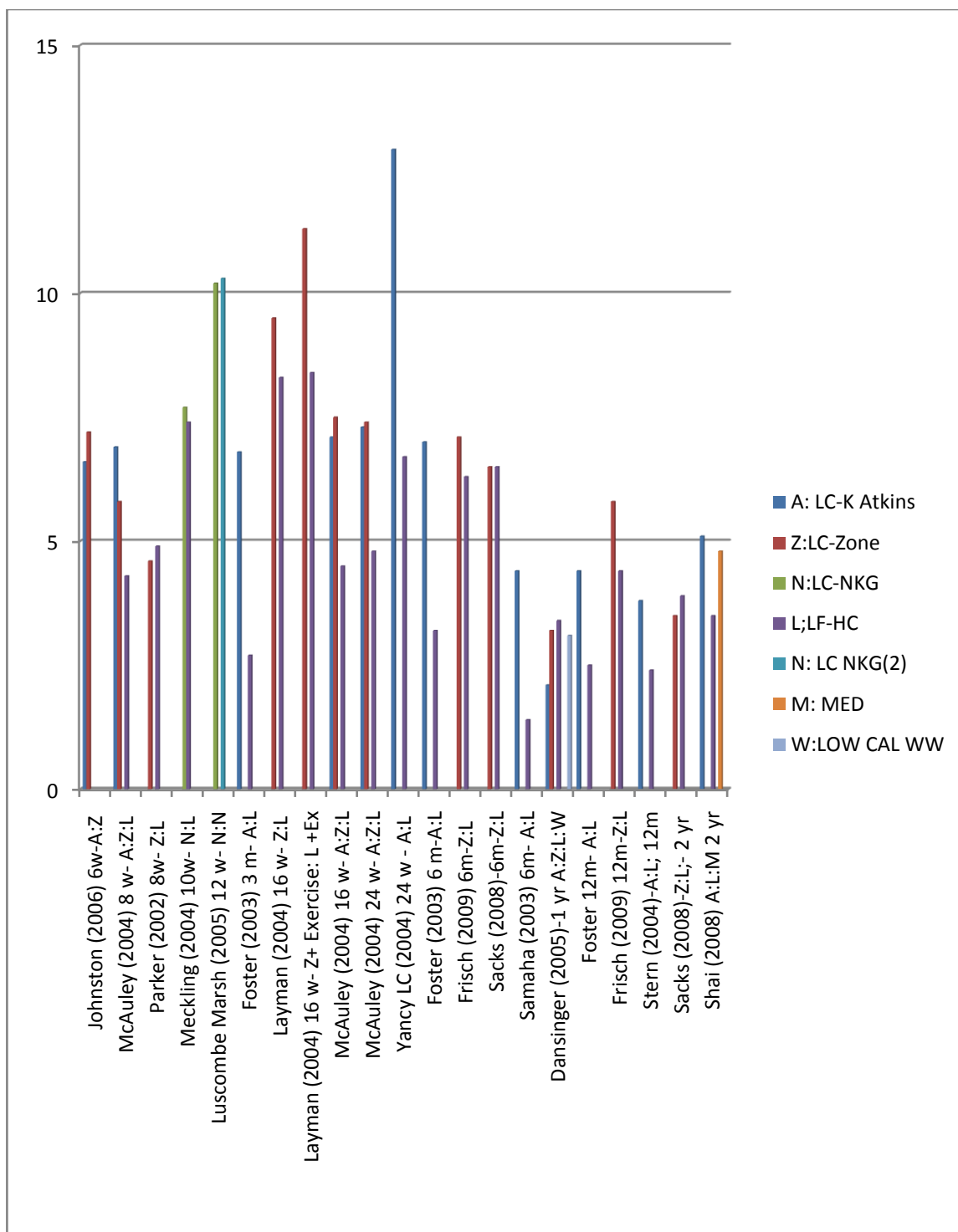


Figure 2: Percentage of Mean Weight Loss from Baseline for Low-Carbohydrate & Comparative Diets Included In Study – In Order of Intervention Duration

In Yancy, Olsen, Guyton, Bakst and Westman (2004), at 24 weeks, weight loss results shown are the expected mean weight loss data based on a linear mixed effects model. The expected mean weight loss was an average of 12.0 kg (12.9%) in the low-carbohydrate Atkins group is considerably higher than that demonstrated by the other studies that included an Atkins type protocol in the design. It is plausible that the linear mixed effects model used is not comparable with the method of assessing weight loss differential in the other studies and that the weight loss recorded may be overstated.

The Atkins diets in Samaha et al. (2003) generated a weight loss marginally below 5% of 4.4% at six months. As the participant group in Samaha et al. (2003) and in the follow-up study Stern et al. (2004) at twelve months included morbidly obese individuals with baseline weight of 130-132 kg as compared to 90-100kg for the other studies, a lower percentage weight loss may be expected. Hence apart from a few exceptions, most of the studies suggest that in the short to medium term of up to six months lowering carbohydrate intake may enable clinically meaningful weight loss of 5-10%, though in the case of morbid obesity, these levels of weight loss are small (Samaha et al. 2003).

Figure 2 and tables 4, 5 & 6, show that in all the selected studies other than Dansinger et al. (2005), Parker et al. (2002) and Sacks et al. (2008), the percentage weight loss results for the restricted-carbohydrate diets were better

than those for the low-fat comparative diets though in many cases the differences within the studies were not regarded as statistically significant.

Longer Term Weight Loss & Weight Loss Maintenance (12 to 24 months)

Mean and percentage weight loss from baseline data for longer-term, low-carbohydrate and comparative low-fat and low-calorie interventions included in the study is shown in Table 6 and represented in Figures 1 & 2. For studies exceeding six months weight loss results were less favourable than for studies with durations of up to six months. Weight loss for the interventions exceeding 12 months and up to 2 years (Table 6) was generally in the range of 2-6% rather than 5-10% for shorter term interventions of up to six months across all the dietary arms. Attrition rates were higher, adherence rates were poorer and weight regain was higher for the longer-term interventions.

In Frisch et al. (2009), sustaining a 400-500 kcal deficit beyond six months was noted to be challenging leading to the possibility of weight regain. Dansinger et al. (2005) noted that at one year, there was poor sustainability and adherence rates for all the diets studied and that adherence level rather than diet type was the key determinant of clinical benefits. In Stern et al. (2004), participants on the one year low-carbohydrate diet maintained most of their 6 month weight loss whereas those on the conventional diet continued to lose weight throughout the year. The final year 1 weight change was -5 ± 8.7 kg in the low-carbohydrate group and -3.1 ± 8.4 kg in the conventional diet group.

Table 6. Low- Carbohydrate & Comparative Diets (Interventions between 12 and 24 months) – Mean & Percentage Weight Loss and Energy Deficit / Day			
	Mean Weight Loss in kg	% Weight Loss	Energy Deficit Per Day (ED) E= estimated (Appendix B2)
Atkins Type Diets			
Dansinger et al. (2005) – 12 months	2.1 kg	2.1% at 52 w	Mean Calorie Reduction (MCR) 138 kcal
Foster et al. (2003) 12 months	4.3 kg	4.4% at 52 w	kcal < than baseline
Shai et al. (2008) 24 months	5.5 kg	5.1% at 52 w	No kcal Restriction (NCR)
Stern et al. (2004) 12 months	5.0 kg	3.8% at 52 w	kcal < LF diet
Non-Ketogenic Zone Type Diets			
Dansinger et al. (2005) -12 months	3.2 kg	3.2% at 52 w	251 kcal
Frisch et al. (2009) 12 months	5.8 kg	5.8% at 52 w	kcal < baseline
Sacks et al. (2008) 24 months	3.3 kg	3.5 % at 104 w	750 kcal
Low-Fat/High-Carbohydrate Diets			
Dansinger et al.(2005) - Ornish (O) 12 months	3.3 kg	3.4% at 52 w	192 kcal
Frisch et al. (2009) 1 year	4.3 kg	4.4% at 52 w	400 kcal
Foster et al. (2003) 12 months	2.5 kg	2.5% at 52 w	Women (Wm): 650 (E) kcal; Men (Mn): 350 kcal (E)
Sacks et al. (2008) LF/AP LF/HP	3.0 kg 3.6 kg	3.2 % at 104 w 3.9 % at 104 w	750 kcal
Shai et al. (2008) 2 Year	2.9 kg	3.2 % at 104 w	Wm: 500 (E); Mn: 200 (E)
Stern et al. (2004) 1 Year	3.1 kg	2.4 % at 52 w	500 kcal/d
Low Calorie Diets			
Dansinger et al. (2005) – Weight Watchers	3.0 kg	3.1% at 52 w	244 kcal/d
Shai et al. (2008)-Mediterranean (M)	4.4 kg	4.8% at 104 w	Wm: 500 (E) kcal/d Mn: 200 (E) kcal/d

The difference between the two diet groups was not significant. Persons on the low-carbohydrate diet who dropped out lost less weight than those who completed the study. In contrast weight loss was not significantly different for those on the conventional diet who dropped out (Stern et al., 2004).

Over a one-year duration, Frisch et al. (2008) found the low-carbohydrate Zone type diet to be as effective as a low-fat/higher-carbohydrate alternative if not more effective for clinically meaningful weight loss. In Sacks et al. (2008), the average weight loss among the 80% of the participants who completed the two year trial was 4kg. However, 14-15% of the participants had a reduction of at least 10% of their initial weight suggesting the significance of individual responses. After 12 months participants generally began to regain weight and by 24 months the weight loss recorded in all the four diet groups namely the two moderate-carbohydrate Zone type diets and the two low-fat/higher-carbohydrate diets was similar (Sacks et al., 2008).

In Shai et al. (2008) for 272 of the participants who completed the 24 month study of the 322 participants who joined the trial, the mean weight loss was 5.5 ± 7.0 kg in the low carbohydrate Atkins group, 4.6 ± 6.0 kg in the Mediterranean diet group and 3.3 ± 4.1 kg in the low fat group. The weight loss differential was considered significant for the comparison between the low-carbohydrate and low-fat groups at 24 months ($P=0.03$) (Shai et al., 2008).

In Foster et al. (2003) and Stern et al. (2004) at 12 months, the differences between low-carbohydrate diets and low-fat alternatives were not found to be significant even though the weight loss results at three and six months favoured low-carbohydrate diets. Hence it is evident that that weight loss differentials between a low-carbohydrate approach and a conventional diet evident at six months may diminish over a period of one year and a low-carbohydrate diet may potentially be less sustainable over a longer term than a conventional diet.

Fat Loss & Abdominal fat as represented by Waist Circumference

The data from the selected studies on fat loss and the impact of the diets on waist circumference is summarized in Appendix C. Of the fourteen studies, three did not measure, comment or report on fat loss data or waist circumference changes (Foster et al., 2003; Samaha et al., 2003; Stern et al., 2004). In all the studies where fat loss and waist circumference changes were measured, a positive association between weight loss and fat loss and/or waist circumference reduction was noted. In seven of the fourteen studies (Dansinger et al., 2005; Johnston et al., 2006; Luscombe-Marsh et al. 2005; Meckling, O'Sullivan & Saari, 2004; Sacks et al., 2008; Shai et al., 2008; Yancy et al., 2004), the differences in fat loss and/or waist circumference results between the different diet arms were not significant.

A few of the studies (Frisch et al., 2009; McAuley et al., 2004; Layman et al., 2005) suggested that lowering carbohydrates may give better fat loss and/or

reduction in waist circumference results than conventional low-fat diets. Layman et al. (2005) noted that fat loss and waist circumference reduction was greatest in the low-carbohydrate group with the higher protein intake and higher intensity and duration of exercise. Meckling et al. (2004) found however that the decrease in lean mass was significant only in the low-carbohydrate group suggesting that a low-fat diet with sufficient protein may better preserve lean mass (Meckling et al., 2004). Hence, from the studies selected, fat loss and a reduction in waist circumference are positively correlated irrespective of diet type; fat loss and preservation of lean mass is enhanced by increased intake of protein and higher levels of exercise. Furthermore, low-carbohydrate diets may generate similar if not greater fat loss and reductions in waist circumference as compared with conventional low-fat diets.

Energy Restriction – Prescribed & Voluntary

Energy restriction both prescribed and voluntary is noted to be a key influence on weight loss achieved. Where no caloric restriction was stipulated at the outset, energy deficit achieved was estimated based on a notional baseline energy level of 2000 kcal per day representing an average energy intake (Appendix B2). All the weight loss diets included irrespective of diet type as shown in tables 4, 5 and 6 suggest that prescribed or resulting, regular and ongoing, energy restriction of 300-750 kcal/d accompanies and potentially underlies weight loss results.

Where diet arms were isocaloric, there was little difference in the weight loss and fat loss results between Atkins and Zone type diets in Johnston et al. (2006) and between two carbohydrate-restricted non-ketogenic diets in Luscombe-Marsh et al. (2005). Moreover, all the weight loss occurred in the twelve week energy restriction phase with no further weight loss occurring during the 4 week energy balance phase highlighting the significance of energy restriction in the weight loss process (Luscombe-Marsh et al., 2005).

In McAuley et al. (2004), even though none of the diets were formally restricted for calories, after eight weeks, the resulting caloric reduction was approximately 450-500 kcal per day for each of the diets. The theory suggested by McAuley et al. (2004) is that with an *ad libitum* dietary protocol, based on the Atkins diet or a Zone type diet, clinically meaningful weight loss may be achieved due to the daily calorie deficit that results from following the protocol. Hence, low-carbohydrate dietary protocols can provide valid weight management options in an *ad libitum* feeding scenario or free-living conditions or where calorie restriction cannot be imposed or complied with. Furthermore, in an *ad libitum* feeding scenario, low-carbohydrate diets particularly the low-carbohydrate Atkins protocol may achieve clinically significant weight loss and often better weight loss than a higher-carbohydrate/low-fat conventional diet over a short to medium term.

Ketogenic versus Non-Ketogenic low-carbohydrate diets

Three studies included in this review permitted a direct comparison between ketogenic and non-ketogenic methods of achieving carbohydrate restriction for purposes of weight management. Where the diet design was isocaloric as in Johnston et al. (2006), the weight loss of 6.3 ± 0.6 kg (6.6% of baseline weight) or fat loss of 3.4 kg for ketogenic Atkins group did not differ significantly by week six from the Zone type group which had weight loss of 7.2 ± 0.8 kg (7.2% of baseline weight) and fat loss of 5.5kg. In McAuley et al. (2004) following an eight week weight loss phase, the weight loss for the Atkins group of 6.9% was similar to that in the Zone Group of 5.8%. Mean fat mass reduction at eight weeks in the Atkins Group was 4.4 kg and 3.1 kg in the Zone Group. Dansinger et al. (2005) included both the Atkins and Zone dietary approaches and noted that the weight loss results at one year were modest but the differences were not statistically significant. Hence the need to severely restrict carbohydrate intake for weight loss purposes may be questioned and a more moderate reduction of carbohydrate may be as effective.

For Atkins type diets whilst caloric prescriptions were not made, there were resulting daily calorie deficits noted. Possible explanations for the lower calorie intake could suggest that subjects may have experienced greater satiety with the permitted liberal portions of protein and fat and/or increased adherence due to the relative simplicity, monotony or novelty of the diet (Foster et al., 2003; Samaha et al., 2003), or ketosis and water loss in the initial phase (Yancy et al.,

2004). Foster et al. (2003) suggested that ketosis was not a likely explanation for the increased weight loss with the Atkins low-carbohydrate diet group as compared with the low-fat group as ketones were not present for most subjects after the first six months. Hence the Atkins approach may provide a viable option for weight management if appropriate to an individual's preferences and health profile.

Gender, Ethnic & Cultural Differences

In Parker et al. (2002), whilst overall weight loss of 5.2 ± 1.8 kg was achieved for both diet groups, this study showed a significant potentially gender related effect as women lost more weight on the Zone type diet as compared with the higher carbohydrate diet (6.0 kg vs. 4.2kg). Similar outcomes were noted for women for fat mass (5.3 vs. 2.8 kg) and abdominal fat (1.3 vs. 0.7kg). Men in the study lost more weight (5.8 kg vs. 4.7kg), fat mass (5.1kg vs. 3.8kg) and abdominal fat (1.7 vs 1.4 kg) on the higher-carbohydrate plan (Parker et al., 2002). This study finds that a higher-protein Zone type diet may have appealed to the women dieters included in the study more than the men (Parker et al., 2002). In Samaha et al. (2003), white subjects lost more weight than black subjects (mean 13 ± 19 kg vs. 5 ± 12 kg, ($P=0.009$) suggesting that weight loss diets and results both in terms of adherence and appeal may have gender related, cultural, ethnic and / or genetic influences.

Impact of Higher Protein Levels implicit in Low-carbohydrate Diets

Lower-carbohydrate diets have generally implied higher protein intake (up to 30% of energy intake) as compared with higher-carbohydrate conventional diets where the protein intake is approximately 15% of energy intake. In Luscombe-Marsh et al. (2005), for two groups with carbohydrate intake restricted to 30% of energy, the subjects' satiety levels were higher for the group with higher protein intake of 40% as compared with group with protein intake of 20% ($P=0.02$). Luscombe-Marsh et al. (2005) highlight that higher levels of protein intake may improve satiety levels and reduce the amount of food desired at the next meal.

Results from Layman et al. (2005) suggest that with a daily caloric restriction of 20-30%, reduced carbohydrate intake and exercise of sufficient intensity, both weight loss and fat loss can be enhanced by consuming higher protein levels of up to 1.6g per kilogram of body weight per day (Layman et al., 2005). Hence carbohydrate restriction together with adequate intake of protein and appropriate exercise would appear to support weight management and fat loss.

Quality of Carbohydrates and Related Food Choices – Nutritional Value; Level of Refining and Processing; Glycemic Index and Load; Dietary Fibre Levels.

A few of the studies included in this review considered the impact of the quality of macronutrient and food choices on weight loss, caloric values, hunger, satiety and cravings. In Meckling et al. (2004) both the low-carbohydrate and the low-

fat groups were advised to eliminate fried foods, high fat and high sugar foods, limit intake of breads, pastas, rice and desserts; eliminate intake of candy, dried fruit, sweetened soft drinks and sugar and encouraged to increase intake of vegetables, lean meats, eggs and nuts. Sacks et al. (2008) re-iterated that recommending inclusion of foods with a low-glycemic index may influence weight loss.

In Luscombe-Marsh et al. (2005), saturated fat was restricted to 10% of energy and fibre for both low-carbohydrate non-ketogenic diets were 21 and 27 grams per day respectively. Sacks et al. (2008) corroborate that prescribing a minimum intake of dietary fibre and a limit to the intake of saturated fat and cholesterol may support the weight loss process (Sacks et al., 2008). In Meckling et al. (2004), the low-fat/ high-carbohydrate group did not meet targets for carbohydrate and fibre intake whilst the Zone group were closer to achieving the fibre targets set for the high-carbohydrate group and achieved relatively better weight loss results. The authors conclude that the high-carbohydrate group may have had better results if they had better instruction with regard to the type of fruit, vegetables and wholegrain cereal included in their diet. Hence weight loss may be influenced by both the quality and quantity of macronutrient intake – carbohydrates, protein and fat; the level of saturated fat intake; the level of fibre intake; the glycemic index of foods and the glycemic load of meals and specifically the limiting of high-sugar and high-fat foods.

Low-carbohydrate Diets and Nutritional Adequacy

A few of the studies included, evaluated the nutritional adequacy of the diets. In Johnston et al. (2006), the Zone type diet was found to have $\geq 67\%$ of the US Recommended Daily Amounts (RDA) for the micronutrients whilst for the Atkins type diet fibre, vitamin E, folate, iron, magnesium and potassium were $<67\%$ of RDA. Hence a daily multivitamin and mineral was included in the protocol.

Meckling et al. (2004) who studied a more moderate reduction in carbohydrates as compared with the Atkins type protocol, shows that subject to the overall attainment of sufficient energy reduction, the exclusion of fruits, whole-grain breads and pastas nutrient rich with their vitamin, mineral and antioxidant content as required by some of the very low-carbohydrate dietary protocols may not be essential to achieve statistically meaningful weight loss. This study highlighted some significant differences between the diet groups related to nutritional adequacy despite similar levels of energy restriction. The low-carbohydrate regime caused deficiencies in calcium, magnesium, iron, vitamin D, folate and Vitamin B6 whilst the low-fat diet caused deficiencies in calcium and vitamin E requirements.

In Meckling et al., 2004, as highlighted by the authors, short-term nutritional shortfalls in the interest of weight management may be tolerated but for the longer-term, nutritional adequacy must be catered for by means of adequate nutrient supplementation. The highlighted studies confirm that with energy

restriction and/or macronutrient manipulation to achieve energy restriction, nutritional inadequacies must be assessed and insured against either via dietary adjustment and/or nutritional supplementation. Furthermore, the inclusion of a daily multivitamin supplement which is usually prescribed by the Atkins diet protocol may be both necessary and prudent during the restricted carbohydrate weight management protocol.

Low-carbohydrate Diets and Exercise

Duration and intensity of exercise and activity levels are likely to impact on the creation of a sufficient energy deficit on a daily basis relevant for weight loss. Hence, in weight loss studies, inadequate measurement and reporting of exercise and/or activity levels could be a confounding factor whilst assessing results. This was the case for three of the fourteen studies included in the review. For the remaining eleven studies, other than for Layman et al. (2004), activity levels either remained constant during the trial and/or did not differ significantly between the diet groups.

Layman et al. (2004) compared Zone type diets with and without the inclusion of exercise to a low-fat/higher-carbohydrate conventional diet protocol with and without exercise. Exercise in the control groups averaged <100min per week against the recommendation of 30 minutes of walking 5 days a week. The 'Exercise' groups were also recommended 30 minutes of walking 5 days a week plus 30 minutes of resistance training and stretching 2 days/week. The higher

exercise group's compliance was supervised and averaged more than 200 minutes per week. The low-carbohydrate group with higher exercise levels achieved the largest relative weight loss at 11.2%. The low-carbohydrate control group with less exercise had weight loss of 9.5%. The higher-carbohydrate group with higher exercise levels had weight loss of 8.4% whilst the high-carbohydrate control group with less exercise achieved weight loss of 8.3%. Taking the two higher exercise groups together the average reduction in fat mass was 7.2 ± 0.7 kg whereas the lower non-supervised exercise groups reduced body fat by 5.5 ± 0.5 kg ($P < 0.05$).

Higher protein intake, lower carbohydrate intake and supervised exercise produced a 21.4% reduction in absolute body fat whilst the higher carbohydrate group without supervised exercise had a 12.8% reduction in body fat. A similar pattern was evident for changes in abdominal or trunk fat. Layman et al. (2004) highlights the additive effects of the low-carbohydrate / high-protein diet and exercise on body composition with significant main effects of diet ($P < 0.01$) and exercise ($P < 0.001$). Hence with moderate restriction of carbohydrate and appropriate levels of protein intake, exercise may enhance weight loss and fat loss in the short to medium term.

Hunger, Satiety & Well Being

Five of the fourteen studies included in this review assessed or commented on hunger, satiety or well being indicators. For Atkins type diets, McAuley et al.

(2004) highlight that enhanced satiety and reduced appetite may be due to the ketonuria associated with carbohydrate restriction. Samaha et al. (2003) note that higher satiety for Atkins type diet may be associated with increased intake of protein and fat. Sacks et al. (2008) used questionnaires to ascertain satiety, hunger, diet satisfaction at specific points in time but found similar results for the two zone type and two low-fat diet groups.

In Luscombe-Marsh et al. (2005), for two non-ketogenic low-carbohydrate diet groups, the higher protein group had more favourable hunger responses and more favourable maintenance of the thermic effect of food (TEF), potentially highlighting the greater satiating effect of protein. Subjects in the higher protein group did desire to eat less at both week 0 and week 16 (main effect of diet, $P=0.02$). There was significant reduction in the 3-hour hunger response ($P=0.018$); and a trend after sixteen weeks, for a reduced desire to eat ($P=0.06$) and a reduced amount desired to be eaten ($P=0.07$) (Luscombe-Marsh et al., 2005).

Johnston et al. (2006) noted improved hunger ratings from “no particular feelings” to “satisfied” ($P=0.078$) for both the Atkins type diet and the Zone type diet included in the study. The hunger indicators did not differ between the two groups suggesting that it may be the protein level in the diet rather than the extent of carbohydrate restriction that potentially affects hunger levels. Based on a “profile of mood states” (POMS) questionnaire used to assess six distinct

mood states, feelings of 'vigour-activity' were greater for the Zone type diet as compared with the Atkins diet ($P=0.025$) at week 5. The other mood indicators such as 'fatigue-inertia', 'depression-dejection', and 'anger-hostility' did not differ between the diet groups. This suggests that within the context of a higher-protein intake, lower-carbohydrate intake levels may potentially affect the desire to be physically active, a behavioural response that may affect obesity states in the long run. Hence the implied higher protein levels implicit in lower-carbohydrate diets may be significant for longer-term adherence to the diet plan by promoting satiety, and deflecting feelings of hunger. Additionally it may be appropriate to monitor the effects of lowering carbohydrates on energy levels as part of a weight management plan.

Attrition & Adherence, Support & Supervision

Most of the studies included in the review other than Layman et al. (2005) included data on withdrawals and dropouts. However for many of the studies, withdrawals, attrition and adherence were not found to be diet related. Dansinger et al. (2005) observed a strong curvilinear association between self-reported dietary adherence and weight loss ($r=0.6$; $P<0.001$) and that participants in the top tertile of adherence lost 7% of weight. Higher discontinuation rates were noted for both the Atkins and the Ornish low-fat groups as these may too extreme relative to the Zone and Weight Watchers group. In addition Dansinger et al. (2005) noted that self-reports of dietary

adherence decreased in relation to time and to a similar extent in each of the diet groups studied.

Sacks et al. (2008) noted that diminished adherence occurred between six months and 2 years as is typical in weight loss trials. They further highlight that regular attendance at counselling sessions helps with weight loss and prevention of weight regain. Frisch et al. (2009) showed that continuous contact with participants reduced drop-out rates and improved compliance. Samaha et al. (2003) found that subjects in the low-carbohydrate Atkins group attended more dietary counselling meetings than the low-fat group and that the differences in attrition were statistically significant at three months ($P=0.03$) in favour of the low-carbohydrate approach but not at six months.

In Foster et al. (2003), the percentage of dropouts at 3, 6 and 12 months was higher for the conventional low-fat group (30, 40 and 43% respectively) than in the low-carbohydrate Atkins group (15, 27 and 39%) but these differences were not significant. Whilst there are mixed results as to whether the adherence rate was higher for the low-carbohydrate diet or the low-fat approach, overall based on the studies included in this review, dietary adherence and regular counselling influences the extent of weight loss and the prevention of weight regain.

Adverse Effects & Safety

Relevant results from the included studies are collated in Appendix D. Yancy et al. (2004), over 2 weeks, reported a greater level of adverse effects in the low-carbohydrate Atkins diet group as compared with the low-fat diet group as shown in Table 7.

Table 7- Adverse Effects: Yancy et al. (2004)

Adverse Effect	Low –CHO Group	Low-fat Group	Significant
Constipation	68%	35%	YES-P<0.001
Headache	60%	40%	YES-P=0.03
Halitosis	38%	8%	YES-P<0.001
Muscle Cramps	35%	7%	YES- P<0.001
Diarrhoea	23%	7%	YES – P=0.006

The authors suggest that such symptomatic adverse effects that occur at the start of low-carbohydrate diets are short-lived and may be reduced and managed by an increase in fluid intake, dietary inclusion of low-starch vegetables, bouillon and a daily multivitamin and mineral supplement (Yancy et al., 2004). Layman et al. (2005) for the Zone Diet, Luscombe-Marsh et al. (2005) and Meckling et al. (2004) for low-carbohydrate non-ketogenic diets, reported no adverse effects or events.

The impact of low-carbohydrate diets particularly the Atkins type diet on renal health and bone-turnover and inflammatory markers were not consistently assessed across the studies reviewed. Dansinger et al. (2005) who included

both an Atkins diet and a Zone type diet in their study design reported no evidence of clinically significant adverse renal effects. Johnston et al. (2006) found that the arachadonic acid: eicosapentanoic acid ratio (AA: EPA) was nearly 90% higher in the Atkins group as compared with the Zone group ($P=0.038$) associated with increased inflammation, a factor that could be monitored in future when the Atkins diet is the preferred dietary option.

Hence the studies included in this review have not shown any significant adverse side-effects or safety issues related to non-ketogenic low-carbohydrate diets including the Zone type diets. Atkins type diets may generate short-term adverse effects that can managed with appropriate actions or precautions. Effects of lowering carbohydrates, particularly with respect to the Atkins type diet on, bone turnover, renal health and inflammatory markers are potentially significant end-points that have been omitted from most of the studies included.

Lipid Control Results

Most of the studies selected reported or commented on the impact of the dietary protocols on the main cholesterol markers - TC, LDL-C, HDL-C and TAG as shown in Appendix E. The results from the studies, including percentage or actual levels of lipid marker change where identified, are summarised at a high level between the low-carbohydrate ketogenic and non-ketogenic diets in Table 8 and the higher-carbohydrate/low-fat comparative and /or control diets in Table 9.

TABLE 8: CHANGES IN BLOOD LIPID LEVELS WITH LOW-CARBOHYDRATE DIETS							
Study	Year	Duration	TC	LDL -C	HDL-C	TAG	
LOW- CARBOHYDRATE KETOGENIC (LCK)- ATKINS (A)							
Dansinger A	2005	1 year	ND	↓ NSS	↑	↔	
Foster A	2003	1 year	ND	↔	↑	↓ > LF	
Johnston A	2006	6 w	ND	↑ 5 dieters ↓ 4 dieters	↓ 9%	ND	
McAuley A	2004	8 w	ND	↓ < HP & HC	↑	↓	
Samaha A	2003	6 m	↔	↔	↔	↓ 20±42%	
Shai A	2008	2 year	TC:HDL ↓ 20%	↔	↑ 0.22 mmol /l.	↓ -0.27 mmol/l	
Stern A	2004	1 year	↔	↔	↓	↓ > LF	
Yancy A	2004	24 w	ND	↑ 0.04 mmol/l	↑ 0.14 mmol/L	↓ -0.84mmol/L	
LOW CARBOHYDRATE NONKETOGENIC (N)– 50-100g C							
Meckling N	2004	10 w	↔	↔	↑ +0.14mmol/L	↓ -0.4	
Luscombe- Marsh (LF/HP) N	2005	12 w	↓ 6.6±1.4%	↓ 3.4±1.9%	↑ 6.8±2%	↓ 23.1±3.6%	
Luscombe-Marsh (HF/SP) N	2005	12 w	↓ 6.6±1.4%	↓ 3.4±1.9%	↑ 6.8±2%	↓ 23.1±3.6%	
LOW- CARBOHYDRATE ZONE (Z) TYPE DIETS							
Dansinger Z	2005	1 yr	ND	↓	↑	↔	
Frisch Z	2009	6m& 1yr	↔	↔ ↔	↔	↓ 14% ↓ 7%	
Johnston Z	2006	6 w		↑ 2 dieters ↓ 8 dieters	↓ 9%	ND	
Layman (HP) Z Layman (HP) Z+EX	2005	16 w	↓ 3.7%	↓ 1.7%	↑ 0.01± 0.03 mmol	↓ 20.2%	
McAuley Z	2004	8 w	ND	↓	↑	↓	
Parker Zone Z	2002	8 w ER	↓	↓	↔	↓	
Sacks (LC/HF) Z	2008	24 m	↓ 1%	ND	↑ 9%	↓ 12-17%	
<p>KEY : ↓=reduced; ↑= increased; ↔= No significant change, A= Atkins; C= carbohydrates; HC= high carbohydrate; ER= energy restriction; EX=exercise; HDL-C= high density lipoprotein; HF= high fat; HP= high protein; kcal= kilocalories; L= low-fat/high carbohydrate; LC= Low-carbohydrate; LDL-C=low density lipoprotein cholesterol; M= Mediterranean diet; m=months; mmol/l= millimoles per litre; Mn=Men; N= low carbohydrate nonketogenic; NCR= No Calorie Restriction; ND=No Data; NSS= Not statistically significant; TAG= triglycerides; TC= total cholesterol; w =weeks; Wm= Women; W= Weight Watchers diet; yr=year; Z= Zone</p>							

TABLE 9: CHANGES IN BLOOD LIPID LEVELS WITH LOW-FAT / HIGH CARBOHYDRATE DIETS							
LOW- FAT CONVENTIONAL DIETS (L)							
Study	Year	Durat- ion	TC	LDL	HDL	TAG	
Dansinger O	2005	1 year	ND	↓	↔	↔	
Foster L	2003	1 year	ND	↔	↑	↓	
Frisch L	2009	6m, 1y	↑	↔ ↔	↓ ↑	↔ ↔	
Layman L Layman L +EX	2004	16 w	↓ 9.2%	↓ 10.4%	↓0.08± 0.03 mmol	↓5.2%	
McAuley HC	2004	8 w	ND	↓ < HP	↑ < HF/HP	↓ < HF/HP	
Meckling L	2004	10 w	↓ -1.6mm	↓ -1.3mm	↓ -0.3	↓ -0.4	
Parker L /LP	2002	8 w	↓ < HP	↓ < HP	↔	↓	
Sacks L/HC	2008	24 m	↓ 5%	ND	↑6%	↓12-17%	
Samaha L	2003	6m	↔	↔	↔	↓2±28%	
Shai L	2008	2 year	TC:HDL ↓12%	↔	↑+0.16 mmol/l	↓0.03 mmol/l	
Stern L	2004	1 year	↔	↔	↓ > LC	↓	
Yancy L	2004	24 w	ND	↓ 0.19 mmol/L	↑-0.04 mmol/L	↓-0.31mmol/L	
OTHER MODERATE CARBOHYDRATE /LOW CALORIE DIETS							
Dansinger W	2005	1 year	ND	↓	↑	↔	
Shai M	2008	2 year	ND	↔	↑	ND	
COLOUR KEY:			Negative	Neutral	Positive		
KEY : ↓=reduced; ↑= increased; ↔= No significant change, >=greater than; <=lesser than; A= Atkins; HC= high carbohydrate; ER= energy restriction; EX=exercise; HDL-C= high density lipoprotein; HF= high fat; HP= high protein; cholesterol; kcal= kilocalories; L= low-fat/high carbohydrate; LC= Low-carbohydrate; LDL-C=low density lipoprotein cholesterol; M= Mediterranean diet; m=months; mmol/l= millimoles per litre; Mn=Men; N= low carbohydrate nonketogenic; NCR= No Calorie Restriction; ND=No Data; NSS= Not statistically significant; O= low-fat Ornish diet; TAG = triglycerides; TC= total cholesterol; w =weeks; Wm= Women; W= Weight Watchers diet; yr=year; Z= Zone.							

The results are colour coded green to show a positive result, pink to show an adverse change, blue where no significant change was found and white to show areas for which no data (ND) was available. In addition Tables 8 and 9 highlight if lipid markers increased (↑), decreased (↓) or showed no significant change (↔).

LDL Cholesterol (LDL-C)

The studies included in this review show mixed results with respect to the potential effects of lowering carbohydrates on LDL-C as indicated in Tables 8 and 9. Of the eight studies that included Atkins type diets, four showed no significant change, one showed an increase in LDL-C whilst Johnson et al. (2006) showed a split result where LDL-C levels increased for five participants and reduced for four participants. For the three low-carbohydrate non-ketogenic diet arms, LDL-C reduced for two and did not change significantly for one. For the seven studies that included Zone type diets, LDL-C reduced for four, did not change for one whilst for one study no data was available. Johnston et al. (2006) showed a split result where LDL-C reduced for eight participants and increased for two participants.

Johnston et al. (2006) found that over the six weeks of the trial, LDL-C was directly correlated to β -hydroxybutyrate concentrations ($r=0.297$, $P=0.025$) and that the mean β -hydroxybutyrate levels, related to ketone bodies, was 3.6 times

in the Atkins participants as compared with that in the Zone diet participants at week 2 ($P=0.018$) but did not differ at week 6.

Parker et al. (2002) observed a significant time by diet effect in the reduction of LDL-cholesterol ($P=0.009$) with a greater reduction for the Zone diet as compared with the higher carbohydrate comparative diet. McAuley et al. (2005) noted that LDL-C results decreased for individuals on the Zone type diet and the conventional higher-carbohydrate diet but were not consistently lower for the Atkins group. A small number of Atkins dieters had a marked increase in LDL-C. Similarly in Yancy et al. (2004), LDL-C increased by more than 10% in 30% of individuals who completed the study. Hence the mixed results with respect to LDL-C suggests that caution needs to be applied when suggesting the Atkins type diet with potentially higher levels of saturated fat when LDL-C levels are of concern. Similar caution may not be necessary with a more moderate Zone type diet.

HDL Cholesterol (HDL-C)

Most of the studies (nine of the fourteen studies selected) as shown in Tables 8 and 9 indicated an improvement or an increase in HDL-C levels with weight loss following a low or moderate carbohydrate plan - the Atkins diet plan as well as the non-ketogenic diets including the Zone type diets. In three of the studies (Frisch et al., 2009; Parker et al., 2002; Samaha et al., 2003) the HDL-C result was unchanged. In Johnston et al. (2006) an adverse 9 % reduction in HDL-C

is reported for both the Atkins and Zone arms of the trial but no data was available to explain this further. Stern et al. (2004) found that with a one-year Atkins weight loss plan, HDL-C had reduced however the reduction of HDL-C on the comparative higher-carbohydrate conventional diet was greater.

Of the 12 studies that included a low-fat/higher-carbohydrate conventional diet, HDL-C decreased for three, remained unchanged for three and increased for six. Hence lowering calories via reduced carbohydrate intake and/or the resulting weight loss may help in improving HDL cholesterol levels. Similar results may be obtained with a conventional low-fat diet though an increase in HDL-C was more consistent with a low-carbohydrate diet protocol.

Triglycerides (TAG)

A majority of the studies selected showed that weight loss was accompanied by reduced TAG levels for the low-carbohydrate diets – ketogenic and non-ketogenic as well as the higher-carbohydrate /low-fat diets. Foster et al. (2003), McAuley et al. (2004) and Stern et al. (2004) show that fasting TAG reduced for all three diets types - the Atkins, Zone and low-fat/high-carbohydrate groups but reduced to a significantly greater extent with the Zone and Atkins diets as compared with the high-carbohydrate diet. Frisch et al. (2009) over six months and one year, found no significant change in TAG levels from baseline values for the low-fat diet group but found a 14% and 7% reduction in TAG in the low-carbohydrate Zone diet group over six months and one year respectively.

Dansinger et al. (2005) noted no significant change for TAG across the Atkins, low-fat and low-calorie Weight Watchers (WW) dietary designs. These results would indicate reduced TAG may be associated with weight loss and/or calorie reduction irrespective of diet type but could also potentially result from lowering carbohydrate intake.

Endocrine and Hormonal Results- Insulin and Blood Sugar Effects

The hormonal and endocrine results derived from the studies including outcomes relating to blood glucose, glycosylated haemoglobin (HbA1c), insulin levels, insulin sensitivity and insulin resistance measures are summarised in Appendix F. Twelve of the fourteen studies selected have included blood sugar and insulin indicators as outcome measures. All twelve of the studies selected noted that lowering carbohydrate intake diets showed improved glycemic and /or insulin markers.

In five of the twelve studies (Meckling et al., 2004; Sacks et al., 2008; Samaha et al., 2003; Shai et al., 2008; Stern et al., 2004), improvements in glucose and /or insulin markers were better for the lower-carbohydrate diets relative to low-fat and low-calorie dietary designs. The other studies selected have shown that improvements in glycemic and/or insulin results with low-carbohydrate diets are similar to the comparative low-fat or low-calorie diets potentially suggesting that these insulin and blood sugar effects may relate to energy restriction or to the weight loss rather than the macronutrient content of the diet.

Shai et al. (2008) showed that among the diabetic group, a decreased level of HbA1c at 24 months in each of the three low-carbohydrate, low-fat and the Mediterranean diet groups but found that the changes were significant ($P<0.05$) only in the low-carbohydrate Atkins type diet group. The direct effect of an Atkins type low-carbohydrate diet on glycemic control for diabetics particularly the effect on HbA1c was further corroborated in Samaha et al. (2003) and Stern et al. (2004). As HbA1c remains a significant risk factor for diabetes, a dietary consideration in favour of a very low-carbohydrate approach may be relevant.

Dansinger et al. (2005) compared four diet types namely the low-carbohydrate Atkins and Zone diets, the low calorie Weight Watchers and the low-fat Ornish diet. They noted improvements in blood glucose and insulin levels for all four diets at two months, six months and twelve months. Furthermore, the lower carbohydrate Atkins and Zone diets were more likely to reduce insulin in the short-term (up to two months) though the Atkins diet failed to significantly reduce mean fasting insulin levels at one year (Dansinger et al., 2005).

Luscombe-Marsh et al. (2005) studied two non-ketogenic diets with carbohydrate intake restricted to 30% of energy. Results after sixteen weeks showed a decrease in fasting serum insulin by $25 \pm 4.2\%$ ($P<0.001$) for both diet groups, with the main effect of time and a reduced insulin resistance index

(HOMA) of $34 \pm 8.8\%$ ($P < 0.001$). Johnston et al. (2006) found that insulin sensitivity was significantly improved with both the Atkins and Zone type diets.

Several studies as shown in Appendix F (Dansinger et al., 2005; Foster et al., 2003; Frisch et al., 2009, McAuley et al., 2004; Parker et al., 2002; Shai et al., 2008) show that glycemic control and/or insulin levels decreased significantly in all the diet groups with no significant differences between the groups, potentially connecting improved insulin levels to reduction in calories consumed and/or weight loss.

Hence, lowering carbohydrate in the diet may support favourable changes for one or more of the following - blood glucose, HbA1c, insulin levels, insulin sensitivity and insulin resistance. The Atkins very low-carbohydrate protocol has shown to be particularly beneficial for glycemic control for diabetics. Additionally, as compared with low-fat diets, lowering carbohydrates may be at least as beneficial if not more favourable for achieving improved blood glucose and insulin sensitivity.

Hypertension

Hypertension is one of the outcomes relevant to metabolic syndrome and potentially affected by obesity and diet. Ten of the twelve studies as shown in Appendix G found that both the lower-carbohydrate diet as well as the higher-carbohydrate alternative show favourable blood pressure (BP) results. The diets

caused a reduction from baseline in both the systolic blood pressure (SBP) and/or diastolic blood pressure (DBP) with no significant differential effect between the diets indicating a potential link between energy restriction and/or weight loss and BP.

Frisch et al. (2009) found that SBP at twelve months was significantly higher in the low-fat group as compared with the low-carbohydrate group. Hence whilst improvements in blood pressure markers may be a result of calorie restriction and/or weight loss achieved, lowering carbohydrates and related weight loss achieved does appear to support the improvement in hypertension markers.

CHAPTER 5- DISCUSSION

This study focused on dietary protocol that lowered carbohydrate intake levels from the recommended carbohydrate levels of 55-60% in a conventional or low-fat/higher-carbohydrate diet. The study has included very low-carbohydrate ketogenic Atkins type diets with carbohydrate intake of 20-50 g/d and interventions with more moderate restriction of carbohydrates including the Zone type diet where carbohydrates are limited to 40% of daily energy intake were also included.

This review confirms that in the short-term, for periods from six weeks to six months, with a prescribed or resultant calorie deficit per day of 300-750 kcal or 30% of baseline energy intake, clinically meaningful weight loss of between 5-10 kilograms or between 5-10% of initial weight may be achieved with low-carbohydrate diet plans. Longer-term studies included in this review show that weight loss slows down considerably and is in the range of 2-5 kilograms (2-6 %) over twelve to twenty four months.

The review also shows that lowering carbohydrates via the Atkins and Zone type diets, together with the resulting calorie reduction, compare favourably with low-fat/higher carbohydrate diets, generating better if not similar results for weight loss, fat loss, lipid markers, blood sugar and insulin markers and hypertension. A reservation was noted was in relation to the Atkins type diet and LDL-C for which, results were mixed and potentially adverse relative to the

conventional low-fat diet. Additionally, the results show that other influences may work in concert with lowering carbohydrate intake to generate favourable weight loss changes and improved metabolic health. These include sufficient levels of protein intake; adequate intake of good fats; avoidance of refined sugars and processed foods; appropriate behavioural changes including adequate activity levels.

The results of this review suggest that lowering carbohydrates may provide nutritional advisors with a valid short-term obesity management tool subject to individual preferences and health profile. More caution is required for longer-term use of low-carbohydrate Atkins type diet plans with greater monitoring and management of inflammatory markers, bone health, renal health, impact on LDL-C and nutritional adequacy. Consequently Public Policy on recommending low-carbohydrate diets as a treatment plan for obesity management may not be justified until additional research is undertaken on the longer-term implications of a low-carbohydrate dietary protocol.

The weight loss results shown by this study are in line with that expected in standard behavioural weight loss programs of up to six months as noted by Wing and Phelan (2005) who suggest that such participants lose 7-10kg (7-10%). Despres et al. (2001) suggest that a 5-10% weight loss is regarded as clinically significant in reducing the risk of diabetes and CVD however this level of weight loss may not be sufficient for an obese and particularly a morbidly

obese individual as suggested in Samaha et al. (2003). Pharmacological and particularly surgical options may be more effective options for morbid obesity. Bond et al. (2009) note that for severely obese individuals ($\text{BMI} \geq 40\text{kg/m}^2$ or $>100\text{pounds}$ overweight), bariatric surgery is the most effective long-term weight loss strategy with average expected weight loss of 25%. By comparison, behavioural weight loss treatments including dietary therapy may typically generate weight loss of 10% (Bond et al., 2009). The UK National Health Service [NHS], National Institute for Health and Clinical Excellence [NICE] (2006), Clinical Guidelines 43 for Obesity (NICE, 2006) recommends bariatric surgery to treat morbid obesity.

As with previous systematic reviews defining a 'low-carbohydrate' diet together with determining inclusion criteria was challenging and remains subject to debate (Adam-Perrot et al., 2006; Boucher et al. 2008; Westman et al., 2003; Westman et al., 2007). In the systematic reviews undertaken by Hession et al. (2008) and Nordmann et al. (2006) high-protein, ketogenic diets with carbohydrate content of less than 20-50g/d and low-carbohydrate diets with carbohydrate content of $\leq 60\text{g/d}$ were included in the review. Bravata et al. (2003) included 107 studies with 94 interventions reporting data for 3268 participants. Of these, 663 participants received diets with a carbohydrate content of $\leq 60\text{g/d}$ of whom only 71 received $\leq 20\text{g/d}$ of carbohydrates. The lack of a clear definition of a low-carbohydrate/ higher protein diet has meant that study designs are not consistent nor are sufficiently robust. Hence

conclusions from systematic reviews and their scope to influence public policy on the effectiveness of carbohydrate restriction remain inconsistent (Hession et al., 2008).

RCTs on the subject of lower-carbohydrate diets have focused on the low-carbohydrate Atkins type ketogenic diets or more moderate carbohydrate restricted Zone type non-ketogenic diets which supports why such diets have been considered in this review. The Atkins and Zone type diets are both popular methods of lowering of carbohydrate intake for weight management purposes, and have and continue to challenge the existing low-fat/higher carbohydrate paradigm. Although these approaches are regarded as “fad diets” (Saltzman et al., 2001), they are supported by popular diet books which provide definition, supporting information, methodology, recipes and testimonials of experience and success of such dietary protocols and have both enabled and persuaded the scientific community to test these protocols more rigorously using RCTs. Hence reviewing the scientific evidence for effectiveness of the popular Atkins and Zone type protocols in the context of a weight management protocol is relevant for clinical practice of a nutritional therapist and lends to both internal and external validity of this study.

This review found that lowering carbohydrates supported favourable changes for hormonal and endocrine markers (blood glucose, HbA1c, insulin levels, insulin sensitivity and insulin resistance) and lipid control (HDL-C, TAG). The

Atkins diet was noted to be particularly beneficial for the glycemic control for diabetics, however showed mixed results for LDL-C, potentially due to higher levels of saturated fat intake. Hence caution was indicated when an Atkins type diet is considered for individuals with raised LDL-C. Other studies noted similar results for the Atkins type weight loss diet. Hession et al. (2008) and Nordmann et al. (2006) cover thirteen very low-carbohydrate, Atkins type interventions and support the view that low-carbohydrate diets are at least as effective if not better than comparative low-fat diets both over six months and over a year for management of obesity and related CVD risk.

Volek et al. (2009), compared two hypocaloric (~1500kcal) diets - an Atkins type low-carbohydrate diet (% carbohydrate: fat: protein=12:59:28) with a low-fat diet (LFD) (56:24:20) in 40 subjects with atherogenic dyslipidemia. Whilst both interventions improved several metabolic results, the low-carbohydrate subjects had consistently reduced glucose (-12%); insulin concentrations; (-50%); weight loss (-10%); reduced adiposity (-14%); more favourable TAG (-51%); HDL-C (13%); postprandial lipemia (-47%) and improved LDL particle distribution. Gardner et al. (2007), in a twelve month randomized trial noted that premenopausal women following the Atkins diet lost more weight and had more improved metabolic factors than women assigned to the Zone diet, and low-fat/higher-carbohydrate Ornish or Learn diets.

Sharman, Gomez, Kraemer and Volek (2004), during a 2 consecutive six-week energy restricted diet, noted that a low-fat diet was more effective at lowering LDL-C but the low-carbohydrate Atkins type diet was more effective at improving several other outcomes of metabolic syndrome including the decrease in fasting serum TAG, the TAG/HDL ratio, postprandial lipemia, serum glucose and greater weight loss (Sharman et al., 2004). Similarly Nordmann et al. (2006) indicated that LDL-C decreased more for participants randomized to low-fat diets but HDL-C and TAG results were better for individuals following a low-carbohydrate Atkins type diet. It should be recognized that the trials incorporating an Atkins type diet are small in number and often undertaken by and/or sponsored by the Atkins Foundation and individuals connected with the foundation hence creating a potential for bias. However these connections are declared and open to scrutiny and review.

The results from this study specifically endorse the validity of the Atkins type diet as a potential weight management option for individuals who are unable to count and/or control caloric intake or those who may prefer an *ad libitum* dietary protocol. In an *ad libitum* scenario, ketogenic low-carbohydrate diets may cause improved satiety and reduced voluntary food intake. Johnstone et al. (2008) in a four week trial found that in the short term, *ad libitum* food intakes were lower with a very low carbohydrate (4% carbohydrate) as compared with a moderate carbohydrate (35% carbohydrate diet).

Although the Atkins diet appears to promote weight loss without hunger in the short term, potential short-term adverse effects were noted namely constipation, headaches, halitosis, muscle cramps and diarrhoea that were significantly higher than the comparative low-fat diets. It was held that these may be managed with adequate fluid intake, nutritional supplementation and increased vegetable fibre intake (Yancy et al., 2004). The long-term effects of the Atkins type diet on health and disease prevention however are still unknown (Astrup et al., 2004; Gardner et al., 2007) and the sustainability of such a low-carbohydrate diet over a longer term is questionable. Crowe (2005) corroborates that the Atkins type low-carbohydrate diet is not likely to be harmful in the short-term and possibly for up to six months, the benefits may outweigh risks. However, the longer term impact of severe carbohydrate restriction particularly on nutritional adequacy, dyslipidemia markers, renal and bone health requires further research. Hence, in addition to the favourable effects of an Atkins type diet on satiety and appetite, the potential impact of a ketogenic Atkins type diet on lipid markers particularly LDL-C, bone health, kidney function, nutritional adequacy and adverse side-effects would need to be independently assessed prior to recommending such a weight loss plan (Adam-Perrot et al. 2006) .

In addition to low-carbohydrate Atkins type diets, the results of this study also endorse the consideration of more moderate restriction of carbohydrates as required by Zone type diets. Three of the fourteen studies included in the review (Dansinger et al., 2005; Johnston et al., 2006; McAuley et al.; 2004), show that,

as compared with an Atkins type diet plan, similar or better weight loss results may be achieved with a moderate-carbohydrate diet. A further seven studies indicate that non-ketogenic low-carbohydrate diets and/or Zone type diets compare favourably with low-fat diets. Johnston, Tjonn and Swan (2004) in a six week study show that with fat intake held at 30% of energy, a more moderate zone type protocol may be significantly better than a low-fat/higher-carbohydrate conventional diet plan with weight loss of 6% ($P<0.05$) and loss of fat mass of 9 – 11% ($P<0.05$).

Other studies have had similar results with respect to Zone type diets and obesity management. Skov, Toubro, Renn, Holm and Astrup (1999) in a study over six months showed that a Zone type diet resulted in weight loss of 8.9kg (10%) and fat loss of 7.6 kg, significantly higher than that for the low-fat/higher carbohydrate group. In addition fasting plasma triglycerides and free fatty acids had decreased significantly from baseline and as compared with a low-fat diet. Farnsworth et al. (2003) in a study of 12 weeks of energy restriction found that a Zone type diet generated weight loss of 7.9 ± 0.5 kg and fat loss of 6.9 ± 0.4 kg, results that were similar to a group on a higher-carbohydrate conventional diet. Additionally, after weight loss, for the Zone type diet group, the glycemic response and serum TAG decreased significantly more than for the low-fat group ($P<0.05$).

Brinkworth, Noakes, Parker, Foster and Clifton (2004) corroborate the reduction in weight loss results over the longer term and concur with the overall favourable comparison of a carbohydrate restricted diet (CRD) with conventional low-fat/higher carbohydrate diets. They undertook a one-year follow-up of a randomised trial comparing two hypocaloric (~ 1600kcal) diets – a Zone type CRD with a conventional low-fat/higher carbohydrate diet. Brinkworth et al. (2004) found that at week 64, weight loss for the CRD was 3.7 ± 1.0 kg (3.8%) while that for the conventional diet was 2.2 ± 1.1 kg (2.4%) and suggested that the CRD may in the long-term have a better CVD profile than the conventional diet. The results from the review of Zone type diets suggest that there may be no need to reduce carbohydrate levels as drastically as in ketogenic Atkins type diets in order to achieve clinically meaningful weight loss and more moderate carbohydrate restriction as in Zone type diets may be appropriate if they induce and sustain an on-going and regular caloric deficit. As noted for studies on the Atkins type diets, individuals connected with the Foundation supporting the Zone diet may have been involved with trials on the Zone diet but the connections are properly disclosed and open to scrutiny.

Hence this study has shown that for studies under six months as well as for longer-term studies of 12 to 24 months, lowering carbohydrates may provide as good an option if not a better option for weight loss and improvement of CVD risk factors as compared with the conventional low-fat/higher carbohydrate diet. Bravata et al. (2003), conversely, found insufficient evidence to recommend low-

carbohydrate diets for participants older than age 50, for use longer than 90 days or for Atkins type diets with carbohydrate intake of 20g/d or less. The large number and heterogeneity of the studies included in Bravata et al. (2003) may explain the difficulty in arriving at clear conclusions. Bravata et al. (2003) also concluded that weight loss was associated with decreased calorie intake and increased diet duration but not reduced carbohydrate content. This review concurs with the significance of regular daily calorie deficits underlying weight loss and the relevance of diet duration, but focuses on the result that an energy deficit and lowering carbohydrate content are not mutually exclusive and in fact the lowering of carbohydrate intake may successfully result in creating a sustainable energy deficit and provide a valid weight management option.

The reduction of mean weight loss for diet studies exceeding six months noted by this review suggests the occurrence of weight loss plateaux and potential weight regain after a certain time period or weight loss level also recognised by Hession et al. (2008). Roberts, Barnard and Croymans (2008) question why participants in weight loss trials regain weight between 6 and 24 months despite a reported calorie deficit of 300-600 calories. Whilst a possible explanation considered was errors in recording and reporting food intake, a further explanation may involve difficulty and or inability to sustain the calorie deficit for sustained periods of time. Klem, Wing, McGuire, Seagle and O Hill (1997) and Wing and O Hill (2001) in descriptive studies of successful long-term weight loss maintenance from individuals on the National Weight Control Registry (NWCR)

in the US stress the significance of a diet low in fat, regular physical activity, self monitoring, coping skills that enable individuals to respond to cravings and stressful situations in way that maintain dietary restraint. Despite the popularity of low-carbohydrate diets, the NWCR results do not as yet endorse carbohydrate restricted diets (CRD) for successful long-term weight management, a result that potentially warrants further research.

Results from this study indicate the significance of protein intake in conjunction with lowering carbohydrates for favourable weight loss results. The low-carbohydrate studies included in this review have incorporated protein intake of between 25-30% of energy intake for the non-ketogenic low-carbohydrate diets and Zone type diets and whilst not specified, the Atkins type diets have generally implied protein intake in the range of at 30% of energy. By contrast for the low-fat/ higher carbohydrate diets, protein levels were generally close to 15-20%. Two of the studies included (Layman et al., 2005; Luscombe-Marsh et al., 2005) highlight the favourable impact of higher protein levels implicit in restricted-carbohydrate diets on satiety, appetite, weight loss and fat loss. Leidy, Carnell, Mattes and Campbell (2007) corroborate the significance of protein intake and show that a with a 750 kcal/day energy deficit diet for twelve weeks, a higher-protein group consuming 30% protein experiences greater perceptions of satiety and pleasure during energy restriction and lower losses of lean body mass as compared with a group consuming 15% protein of total energy intake although had comparable weight loss.

Clifton, Keogh and Noakes (2008) show that in a 12 week intensive weight loss programme followed by a 52 week follow-up, protein intake was linked to weight change ($P=0.003$) and that higher protein intake confers some weight loss benefit (Clifton et al., 2008). Hence higher protein intake generally implicit in a low-carbohydrate dietary design would appear to be significant in promoting satiety and preserving lean body mass during diet induced weight loss and may be significant for longer term adherence to a low-carbohydrate weight loss plan.

The results suggest that in addition to the quantity of macronutrient intake, the quality and nature of macronutrients may influence obesity management results. Three of the studies included in this review provide perspectives on the nature of carbohydrates and fats permissible in the diet plans for weight loss. In summary these studies recommend the exclusion of high sugar and high fat foods, prescribing minimum intake of dietary fibre, limiting saturated fats and cholesterol, inclusion of low-glycemic carbohydrates and lean protein. Meckling et al. (2004) noted that the Zone type low-carbohydrate diet group who were able to include fruit, vegetable and wholegrain cereals in their diet were better able to achieve the fibre targets set for the high-carbohydrate group and achieved better weight loss results.

Maki, Rains, Kaden, Raneri and Davidson (2007) in a twelve week RCT found that a reduced glycemic load *ad libitum* diet group lost significantly more weight and had better improvement in HDL-C as compared with a low-fat portion

controlled diet group. Conversely Liese et al. (2005) in a two-year study found no association between glycemic index and insulin sensitivity, BMI or waist circumference but found a positive association of fibre intake with the same markers. Howard and Wylie-Rosett (2002) corroborate that a diet high in sucrose of >20% of energy is linked with increased TAG due to increased hepatic secretion as well as impaired clearance of very-low-density lipoprotein. Hence, weight management results are potentially impacted by the quality of carbohydrate and fats included in the dietary protocol. Crowe (2005) concurs that advice to those following a low-carbohydrate diet should promote the reduction of refined 'nutritionally deplete' carbohydrate foods but encourage the inclusion of fruit and high-fibre carbohydrate sources and replace saturated fat intake with mono-unsaturated fats (MUFA) and polyunsaturated fats (PUFA).

The results suggest that lowering carbohydrates particularly to levels required by the Atkins type diet and/or the related prescribed or resulting caloric deficit may potentially cause nutritional shortfalls. These shortfalls may need to be managed and corrected by the use of appropriate supplements. Adam-Perrot et al. (2006) corroborate that low-carbohydrate diets that restrict food choices and recommend generally low intake of fruits vegetables and whole grain products as is required during the early phases of the Atkins diet potentially causes shortfalls in intake of dietary fibre, vitamins, calcium, potassium, magnesium and iron. Whilst short-term nutritional shortfalls may be tolerated, correction of longer-term shortfalls associated with carbohydrate and/or caloric restriction

should be addressed with appropriate nutritional supplements. Crowe (2005) corroborates that when recommending a low-carbohydrate diet, taking a daily multivitamin supplement would be sensible to protect against micronutrient deficiencies.

The studies selected mainly compare lowering carbohydrates with a higher-carbohydrate low-fat design. These reflect the nature of the studies available as RCTs. The studies selected show that low-fat, calorie-restricted, conventional diet may also generate favourable weight loss and favourable lipid change results however lowering fats has potentially led to a situation where good and essential fats have been removed from the diet while high sugar or high sugar substitute foods have been substituted with consequential effects on health. Essential fats are often ignored in low-fat dietary recommendations as is evident from the studies selected. Minimum intake of these essential fats is rarely stipulated in the design of the diets studied.

Research has for some years provided evidence on the benefits of MUFA, the need for some saturated fat and the requirement for dietary intake of essential fats in the form of omega 3 and omega 6 fatty acids (Lichtenstein & Van Horn, 1998). Siri-Tarino, Sun, Hu and Krauss (2010) suggest that the benefits of reducing saturated fats must be evaluated in the context of the replacement macronutrient included. Whilst replacement of saturated fats with PUFA or MUFA may lower CVD risk (Lichtenstein & Van Horn, 1998), there are few

epidemiological or clinical trials that support the replacement of saturated fats by carbohydrates to support CVD markers favourably. Recent dietary guidelines by the USDA (2010) recommend that most of the 20-35% of fat intake recommended should constitute PUFA and MUFA. Hence, when recommending lowering carbohydrates in a weight loss protocol, the quantity and quality of fats to be included is relevant and important.

Siri-Tarino et al. (2010) further re-iterate that a higher intake of carbohydrates particularly refined carbohydrates can exacerbate atherogenic dyslipidemia as a result of raised insulin levels. Whilst the FSA (2006) and USDA (2010) guidelines promote wholegrains over refined carbohydrates, a question remains as to whether the level of carbohydrates recommended ($\geq 55\%$ of energy) is appropriate (Hite et al., 2010) and potentially whether carbohydrate intake levels should be determined based on individual profile and 'carbohydrate sensitivity' (Heller & Heller, 1994).

This systematic review selected RCTs that lowered carbohydrate intake to assess if lowering carbohydrates supports the management of obesity and related disease. RCTs are the "gold standard" for quality of evidence (Hart, 2003). The included studies, however, were heterogeneous in nature which was also noted in previous systematic reviews of dietary studies (Bravata et al., 2003; Hession et al., 2008). Determining recommended dietary protocol for health and/or weight loss from reviews of a range of diverse research studies

designed as RCTs is highly likely to be challenging (Bravata et al., 2003) because of the number of variables and potential confounding factors in the design and application of diets. However by using the data extraction analytical tool as per Appendices A2-A15, some uniformity of analysis was possible and an attempt has been made to draw from this relatively small selection of studies included, sufficient data and concepts towards a theoretical framework.

Furthermore, the dietary studies could not be blinded and the controls were usually an alternative eating plan as opposed to a placebo in a drug trial. Hence, the three-item, five point scale (Jadad et al., 1996) used to assess the quality of RCTs was not appropriate for the dietary studies selected as these were not blinded (Nordmann et al., 2006). The lack of blinding potentially diminishes the quality and validity of the individual trials (Nordmann et al., 2006). It would appear that pharmaceutical options have a greater chance of being approved as weight loss and cardiovascular risk management treatment options as these lend themselves better to double blind RCTs. This is corroborated by the UK NHS obesity guidelines (NICE, 2006) that offers obese patients pharmaceutical options to enable weight loss where behavioural programmes have not succeeded.

RCTs are more easily able to deal with quantitative and tangible variables that can be measured at defined points in time. Apart from dietary and activity variables, obesity, hunger and satiety are potentially affected by variables that

may not lend themselves to convenient measurement within the structure of a dietary RCT. These include daily and regular levels of stress, quality and quantity of sleep, daily and hourly levels of the hormones insulin, glucagon, leptin, ghrelin, growth hormone and cortisol (Healey & Schwartz, 2010; Spiegel et al. 2004). Dietary RCTs are not able to effectively assess the impact of these variables though in some of the studies selected, periodic qualitative and quantitative measures have been used to estimate the effect of some of these variables. These are more easily incorporated in an individualised case study approach where obesity can be managed on a personalised programme. Hence inherent limitations in the applicability of RCTs to dietary and behavioural obesity studies and the complexity of the variables impacting on obesity states affects the completeness of the conclusions derived.

This review has highlighted the additive effects of lowering carbohydrate intake, adequate protein and exercise on weight loss and fat loss. Giannopoulou et al. (2004) noted a modest weight loss of 5% over fourteen weeks with a hypocaloric (600 kcal deficit), reduced carbohydrate (40%), and high monounsaturated fat (40%), moderate protein (20%) diet group. Similar weight loss results were noted for a group with the same diet together with an exercise programme of walking for 50 minutes three times per week. However, visceral adipose tissue loss, generally associated with improvements in insulin sensitivity and glycemic control, was only evident for the exercise group (Giannopoulou et al., 2004).

Slentz et al. (2009) in an RCT evaluating the effects of exercise duration and intensity on visceral fat found that while sedentary controls gained visceral fat, participants who undertook the equivalent of 11 miles of moderate exercise like walking per week prevented accumulation of visceral fat. In addition higher intensity exercise like jogging for 20 miles per week resulted in decreased visceral abdominal fat. Hence the evaluation of the amount and intensity of exercise for the decrease of and/or the prevention of gain of abdominal fat is significant for any weight loss effort and should be considered in conjunction with dietary changes.

This review has highlighted that the sustainability of weight loss diets is likely to be influenced by a variety of outcomes which may include satiety, hunger and well being, adherence and attrition, side effects and safety and supervision and monitoring required. These outcomes have been measured and evaluated inconsistently across the studies selected. Their omission undervalues the quality of the results obtained. The relatively higher protein intake implicit in both the low-carbohydrate Atkins and Zone type diets would appear to increase satiety and reduce hunger whilst sustaining a caloric deficit. The Zone type diet generated a more favourable mood profile and feelings of high energy (Johnston et al., 2006). Bravata et al. (2003) also identified the need for studies of isocaloric diets with differing carbohydrate content to be assessed for symptoms of hunger and tolerability of the diet. Hession et al. (2008)

recommends the use of questionnaires within dietary weight loss studies to assess appetite, mood, and impact on lifestyle.

From the results of this study, adherence rates were generally linked to weight loss success. It was noted that attrition and drop-out rates were high as is common in dietary studies with a RCT design but were not generally diet related. It was further noted that ongoing continuous monitoring improved compliance and reduced drop-out rates (Frisch et al., 2009, Shai et al., 2008). Hession et al. (2008) have also recommended the use of continuous improvement methodology to better manage attrition rates when using RCTs for diet and lifestyle interventions.

This study finds that a higher-protein Zone type diet may suit or be preferred by women dieters as compared with men (Parker et al., 2002) and the Atkins type diet may work better for white subjects more than black subjects (Samaha et al., 2003). This suggests that a weight loss strategy both in terms of choice, adherence and appropriateness may have gender, cultural, ethnic and / or genetic influences. Recently popularised genetic profile tests (MyGenomics, 2012) are also able to corroborate if fat restriction or carbohydrate restriction is more appropriate for an individual. NICE (2006) supports the need for cultural and ethnic sensitivity when suggesting weight loss protocol.

As noted previously, where total cholesterol and or LDL-C levels are high, a high-saturated fat Atkins type diet may not be appropriate whilst a more moderate carbohydrate Zone type diet or a low-fat conventional diet do not indicate adverse results. Additionally, vegetarians and vegans would find it difficult to use the Atkins protocol due the high animal protein content. Lowering carbohydrates may also have particular significance for individuals with an impaired carbohydrate mechanism leading to “carbohydrate sensitivity” or “carbohydrate addiction” and/or “sugar addiction” (Heller & Heller, 1994). In such a scenario, lowering the absolute intake of carbohydrates or the frequency of intake as described by Heller and Heller (1994) may provide an appropriate weight loss and management strategy to manage the resultant chronic hyperinsulinemia. Hence, weight loss plans should be individualised and tailored to address an individual’s health risk profile, genetic susceptibilities, cultural and dietary preferences.

This review is subject to several limitations many of which are in common with similar reviews of dietary studies. The sample size of selected studies is relatively small. The study searches were limited to the PubMed database for English language studies from 2000 to 2010, involving clinical trials for which full text articles were available together with reference lists of articles selected. This process may have introduced some selection bias and /or publication bias (Bravata et al., 2003; Nordmann et al., 2006).

A majority of the studies available for inclusion as well as those selected were of a relatively short duration of up to six months with few studies extending the intervention duration to 12 and 24. There was insufficient follow-up of the short term study results also noted by Bravata et al. (2003) and Hession et al. (2008). This reflects the overall population of clinical trials available on the subject of lowering carbohydrates. It is recognized that studies of such short duration may not adequately reflect a longer-term lifestyle change expected in obesity management.

Any limitations of the individual studies in process, inclusion, structure or results would implicitly be carried forward into the results and observations from this systematic review that aims to combine the process and results of the underlying studies included. All the studies selected required recording and declaration of food intake. Such records of food intake via food diaries are generally subject to error and inaccuracies which may affect the integrity of the results of this study. Assessing behavioural interventions including dietary studies is difficult due to potential inaccuracies in recording food consumption and activity levels. Roberts et al. (2008) note that food frequency questionnaires may not always provide accurate information on energy and macronutrient intake but are better at indicating general dietary patterns. Lichtman et al. (1992) and Goris, Westerp-Plantenga and Westerp (2000) further highlight that self-reported calorie intake is often under-reported in dietary studies.

Not all the studies consider nutritional adequacy or provide sufficient detail on the quality of carbohydrates and other foods permissible on the diet plan significant because the primary culprit in weight gain may not necessarily be the relative quantity of macronutrients but the quality thereof. Not all the studies included in this review incorporate or isolate the effects of exercise on weight loss. Exercise may in many studies be regarded as a confounding factor. Either insufficient detail was provided of the nature and intensity of activity undertaken in order to assess impact on the energy balance equation or studies stated that participants were encouraged to maintain baseline levels of exercise and activity, also noted by Bravata et al. (2003). Most of the studies included in this review report on body composition but the primary focus is weight loss rather than fat loss. Some studies did not provide results on fat loss, waist circumference and preservation of lean mass following caloric restriction thereby diminishing their usefulness in assessing impact on metabolic disease.

The studies selected potentially gave insufficient emphasis to hunger, satiety, well being and/or slowing of metabolism responses caused by food restriction. Whilst these outcomes were included in a few studies, it is plausible that they are key outcomes for any weight management study, contribute to continued adherence to the diets involved and hence should be essential outcome measures. Bravata et al. (2003) concur with the need for additional studies of isocaloric diets where participants are assessed for hunger responses and on the tolerability of the diet.

The assessment of LDL particle size by the inclusion of small low-density lipoproteins as an outcome measure was largely omitted by most of the studies selected. Small low-density lipoproteins are now recognised as a key CVD risk indicator along with triglycerides level and HDL-C markers (Despres et al., 2001). Hession et al. (2008) also highlighted that the studies included in their review failed to investigate changes in the LDL particle size and Sharman et al. (2002) indicate that on a low-carbohydrate/high protein diet, LDL particle size changes from small to large therefore resulting in a less atherogenic profile.

CHAPTER 6 – FUTURE IMPLICATIONS

Future implications from this review relate to potential improvements in the design, data range and scope of future dietary research studies for weight management including those that restrict carbohydrate intake; exploring and establishing methods of sustaining weight loss over a longer term and weight loss maintenance and evaluating the importance of Public Policy on obesity management.

Future weight management studies including those that lower carbohydrate intake should measure changes in body fat, waist circumference and abdominal obesity more clearly, as these have been significantly linked to insulin resistance, metabolic syndrome and chronic heart disease; evaluate the sustainability of a caloric deficit over the longer term; provide improved reporting on hunger, satiety and well-being outcomes as these strongly influence adherence and attrition; explore other reasons for attrition and adherence to assess if reasons for dropping out may be avoided or reduced by better management. In this context, methods to prevent a physiological response of slowing down metabolism in response to sustained caloric deficit or severe carbohydrate restriction should be studied further. Possible methods could involve the concept of calorie cycling and/or cycling of carbohydrate intake levels to break monotony or to prevent weight loss stagnation. Studies that included higher protein levels or very low-carbohydrate levels should measure renal health and bone turnover due to potential health risks identified.

In addition more focused long-term studies should be undertaken to identify critical success factors to achieve sustained weight reduction to healthy BMI levels. Analysis of successful weight management protocol should be undertaken by critically continually reviewing cases from the National Weight Control Registry [NWCR] in the US (as cited in Wing & Phelan, 2005), successful case studies from medical practice, popular diet literature as any successful experience may have the potential to be replicated in a clinical setting.

Although dietary guidelines recommend the lowering of refined and processed foods, greater controls and monitoring should be undertaken with respect to the manufacturing and marketing of high sugar/high fat foods. Stronger public information messages should be made to persuade all individuals, particularly overweight and obese individuals to limit the level of carbohydrate intake including starches to good quality, low glycemic carbohydrates based on their tolerance levels.

Dietary management of obesity and overweight is a field of scientific study where unpublished grey literature and popular diet books have and may continue to push the boundaries of scientific understanding and identify areas which have the potential for more rigorous research. This is evident from the iterative development of the theory from researchers, clinicians and lay people via diet and weight loss books. Considerable insights have been obtained by

these individuals from a synthesis of research studies on feeding, hunger, appetite, digestion and metabolism. Government health agencies should sponsor research by means of RCTs on successful or popular protocol and provide public guidance on dietary changes required to combat obesity. In this context, Crowe (2005) suggests that some of the new “commercial incarnations” of low-carbohydrate diets that incorporate such sensible dietary changes should be promoted by doctors, nutritionists and public health messages (Crowe, 2005).

CHAPTER 7: A PROPOSED THEORETICAL WEIGHT MANAGEMENT

MODEL

Based on a synthesis of findings from this review and consideration of the limitations it may be postulated that weight management should be a tailored, individualised programme that requires the assessment of several key elements. Figure 3 diagrammatically represents a suggested theoretical basis for designing a weight management protocol that may be appropriate for clinical practice.

Weight Management may be regarded as a function of several influences that include energy restriction; carbohydrate Intake – good quantity in keeping with individual carbohydrate sensitivity; protein intake- good quality and sufficient; fats– sufficient MUFA, PUFA , low saturated and trans fats; dis-allowance of refined sugars, processed food, and “junk food”; reduced glycemic load of meals and increased fibre; sufficient diet duration; improved adherence; regular monitoring and supervision; exercise & activity – suitable type, intensity and frequency; adequate sleep and stress management. Desired outcomes are weight loss achieved – absolute and percentage; increased fat Loss ; waist circumference reduction; hunger management; higher satiety levels ; lean mass preservation; TAG reduction; HDL-C increase; Small LDL-C particle reduction; Improved glycemic control and insulin sensitivity; nutritional adequacy; safety and reduced side effects; flexibility in choosing a diet; clear dietary protocol and support ; and adequate diet maintenance plans.

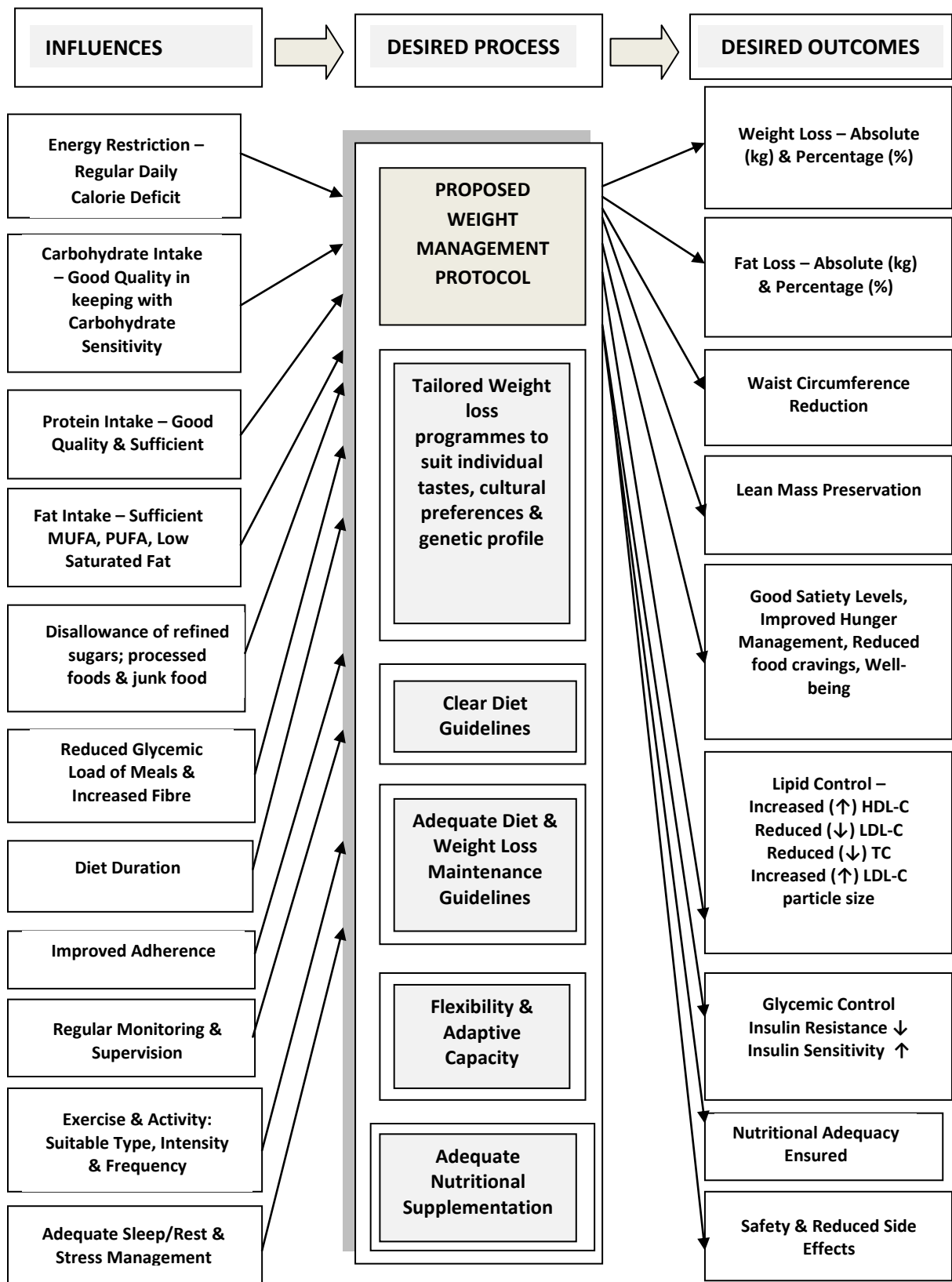


FIGURE 3. A PROPOSED THEORETICAL WEIGHT MANAGEMENT MODEL

The studies selected in this review have measured and commented on many of if not all of the above outcomes. As suggested by the model the tailoring of a weight management strategy in a clinical setting may consider lowering carbohydrates if suitable or preferred by an individual but would need to be done in concert with appropriate recommendations on the other influences on weight management identified and management of any related risks. Glenny, O'Meara, Melville, Sheldon and Wilson (1997) in a comprehensive systematic review on the treatment and prevention of obesity support the use of multi-component strategies for the management of obesity and recommend that interventions that indicate success should be replicated.

The most recent obesity related guidelines for the UK (NICE 2006) and the US dietary guidelines (USDA, 2010) also recommend multi-component interventions that include improved eating behaviour, increased physical activity and reduced energy intake. However they continue to support a low-fat/ higher carbohydrate approach to obesity management with a recent increased emphasis on PUFA and MUFA. Little or insufficient recognition is given to the potential need to reduce carbohydrate intake in keeping with individual carbohydrate tolerance levels; the significance of the glycemic load of meals; or the significance of the level of protein intake.

CHAPTER 8 – CONCLUSIONS

This study endorses a strategy of lowering carbohydrates in the management of mild to moderate overweight and related metabolic disease if appropriate to the preferences and health risk profile of an individual. In the short term of six weeks to six months, 'clinically meaningful' weight loss of 5-10% and an improvement in metabolic risk factors may be expected. Longer-term weight loss with a carbohydrate restricted diet reduces to 2-6 % for periods from 12 to 24 months suggesting that sustaining such weight loss and preventing weight gain may be challenging. A daily caloric deficit in the range of 300-750 kcal/day or 30% of baseline energy, prescribed or resulting from the low-carbohydrate dietary protocol was significant to the weight loss results achieved. Current dietary guidance for obesity management in the UK and the US supports a low-fat/higher carbohydrate approach to obesity management with an emphasis on energy restriction and lowering saturated fat intake. They do not currently support low-carbohydrate diets for health potentially due to uncertainties about long-term suitability of low-carbohydrate diets.

Whilst this theoretical and philosophical review of lowering carbohydrate intakes for the management of obesity and related metabolic disease does not suggest that low-carbohydrate dietary therapy is the best or only way forward, it does question the existing paradigm and status of the conventional low-fat/higher carbohydrate diet as being the most appropriate or most effective option for all

individuals including overweight and obese individuals as is currently being proposed by health advisors in the UK and US.

As a nutritional therapist, there is a case for tailoring weight loss dietary advice based on the format of a theoretical model suggested in this review to suit individual preferences, genetics and medical profile. Sustainability of the diet design and potential for longer term adherence is more significant when recommending a relevant weight loss plan. Some individuals are more easily able to restrict fat intake whilst others are more easily able to restrict carbohydrate intake. Such preferences should be taken into account when designing an appropriate diet plan.

Lowering carbohydrate intake may provide a viable method of calorie restriction particularly for the short to medium term and should be an available choice to individuals for weight management, if appropriate and subject to the management of related risks. More research is required to support the longer-term use of ketogenic Atkins type diets for obesity management but a more moderate reduction of carbohydrates as suggested by Zone type diets may be compatible with recent dietary guidelines issued by health authorities in the US and the UK.

REFERENCES

- Adam-Perrot, A., Clifton, P., & Brouns, F. (2006). Low-carbohydrate diets: nutritional and physiological aspects. *Obesity Reviews*, 7, 49-58. Retrieved from [http://onlinelibrary.wiley.com/journal/10.1111/\(ISSN\)1467-789X/issues](http://onlinelibrary.wiley.com/journal/10.1111/(ISSN)1467-789X/issues)
- Agatston, A. (2003). *The South Beach diet*. London, United Kingdom: Headline Book Publishing.
- Allender, S., & Rayner, M. (2007). The burden of overweight and obesity-related ill health in the UK. *Obesity Reviews*, 8, 467-473. doi: 10.1111/j.1467-789X.2007.00394.x
- American Medical Association [AMA] (1974). A critique of low-carbohydrate ketogenic weight reduction regimens: A review of Dr Atkins' diet revolution. *Journal of the American Medical Association* 224, 1415. Retrieved from <http://jama.jamanetwork.com/journal.aspx>
- Astrup, A., Larsen, T. M., & Harper, A. (2004). Atkins and other low-carbohydrate diets: hoax or an effective tool for weight loss? *The Lancet*, 364, 897-899. Retrieved from <http://www.thelancet.com>
- Atkins, R. C. (2002). *Dr Atkins new diet revolution*. London, United Kingdom: Vermilion.
- Banting, W. (1869). *Letter on corpulence*. Retrieved February 6, 2012 from http://www.subdude-site.com/WebPages_Local/Blog/topics/health/WilliamBanting_LetterOnCorpulence1864.pdf
- Bond, D. S., Phelan, S., Leahey, T. M., O. Hill, J., & Wing, R. R. (2009). Weight loss maintenance in successful weight losers: surgical versus non-surgical methods. *International Journal of Obesity*, 33(1), 173-180. doi:10.1038/ijo.2008.256
- Bouchard, C. (1991). Current understanding of the etiology of obesity: genetic and nongenetic factors. *American Journal of Clinical Nutrition*, 53, 1561S-1565S. Retrieved from <http://ajcn.nutrition.org>
- Boucher, J. L., Benson, G. A., Kovarik, S., Solem, B., & VanWormer, J. J. (2008). Current trends in weight management: what advice do we give to patients? *Clinical Diabetes*, 26(3), 115-120. Retrieved from <http://clinical.diabetesjournals.org>
- Bowling, A. (2002). *Research methods in health*. (2nd ed.). Maidenhead, United Kingdom: Open University Press.
- Bravata, D. M., Sanders, L., Huang, J., Krumholz, H. M., Olkin, I., Gardner, C. D., & Bravata, D. M. (2003). Efficacy and safety of low-carbohydrate diets. *Journal of the American Medical Association*, 289 (14), 1837-1850. Retrieved from <http://jama.jamanetwork.com/journal.aspx>

- Brinkworth, G. D., Noakes, M., Parker, B., Foster, P., & Clifton, P. M. (2004). Long-term effects of advice to consume a high-protein, low-fat diet, rather than a conventional weight-loss diet, in obese adults with Type 2 Diabetes: one year follow up of a randomised trial. *Diabetologia*, 47, 1677-1686. doi: 10.1007/s00125-004-1511-7
- Brownell, K. D., & Stunkard, A. J. (1978). Behavioural treatment of obesity in children. *American Journal of Diseases of Children*, 132, 403-412. Retrieved from <http://archpedi.jamanetwork.com>
- Brownell, K. D., & Wadden, T. A. (1992). Etiology and treatment of obesity: Understanding a serious, prevalent, and refractory disorder. *Journal of Consulting and Clinical Psychology*, 60(4), 505-517. Retrieved from <http://www.apa.org/pubs/journals/ccp/index.aspx>
- Bryngelsson, S., & Asp, N-G. (2005). Popular diets, body weight and health: What is scientifically documented? *Scandinavian Journal of Nutrition*, 49 (1), 15-20. doi: 10.1080/11026480510031990
- Cheuvront, S. N. (2003). The Zone diet phenomenon: A closer look at the science behind the claims. *Journal of the American College of Nutrition*, 22(1), 9-17. Retrieved from <http://www.jacn.org>
- Clifton, P. M., Keogh, J. B., & Noakes, M. (2008). Long-term effects of a high-protein weight-loss diet. *American Journal of Clinical Nutrition*, 87, 23-29. Retrieved from <http://ajcn.nutrition.org>
- Cook, D. J., Mulrow, C. D., & Haynes, R. B. (1997). Systematic reviews: synthesis of best evidence for clinical decisions. *Annals of Internal Medicine*, 126 (5), 376-380. Retrieved from <http://annals.org/journal.aspx>
- Cordain, L. (2002). The nutritional characteristics of a contemporary diet based upon paleolithic food groups. *Journal of the American Nutraceutical Association*, 5 (3), 15-24. Retrieved from <http://thepaleodiet.com/wp-content/uploads/2011/02/The-Nutritional-Characteristics-of-a-Contemporary-Diet-Based-Upon-Paleolithic-Food-Groupsabstract4.pdf>
- Crombie, I. K. (1996). *The pocket guide to critical appraisal*. London, United Kingdom: BMJ Books.
- Crowe, T. C. (2005). Safety of low-carbohydrates. *Obesity Reviews*, 6, 235-245. doi: 10.1111/j.1467-789X.2005.00196.x
- Dansinger, M. L., Gleason, J. A., Griffith, J. L., Selker, H. P., & Schaefer, E. J. (2005). Comparison of the Atkins, Ornish, Weight Watchers, and Zone diets for weight loss and heart disease reduction. *Journal of the American Medical Association*, 293 (1), 43-53. Retrieved from <http://jama.jamanetwork.com/journal.aspx>

- Davis, N. J., Tomuta, N., Schechter, C., Isasi, C. R., Segal-Isaacson, C. J., Stein, D., ... Wylie-Rosett, J. (2009). Comparative study of the effects of a 1-year dietary intervention of a low-carbohydrate diet versus a low-fat diet on weight and glycemic control in type-2 diabetes. *Diabetes Care*, 32 (7), 1147-1152. doi: 10.2337/dc08-2108
- Davis, R. B., & Turner, L. W. (2001). A review of current weight management: research and recommendations. *Journal of the American Academy of Nurse Practitioners*, 13(1), 15-19. Retrieved from <http://www.aanp.org/publications/jaanp>
- Department of Health [DOH] (1991). *Report on health and social subjects 41. Dietary reference values for food energy and nutrients for the United Kingdom. Report of the panel on dietary reference values of the committee on medical aspects of food policy*. Norwich, United Kingdom: The Stationery Office.
- Department of Health [DOH] 2012. *Facts and figures on obesity 30 April 2012*. Retrieved September 14, 2012 from <http://www.dh.gov.uk/health/2012/04/obesityfacts/>
- Despres, J., Lemieux, I., & Prud'homme, D. (2001). Treatment of obesity: need to focus on high risk abdominally obese patients. *British Medical Journal*, 322, 716-720. Retrieved from <http://www.bmj.com>
- Downs, S. H., & Black, N. (1998). The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. *Journal of Epidemiological Community Health*, 52, 377-384. Retrieved from <http://jech.bmj.com>
- Dukan, P. (2010). *The Dukan diet*. London, United Kingdom: Hodder & Stoughton.
- Farnsworth, E., Luscombe, N. D., Noakes, M., Wittert, G., Argyiou, E., & Clifton, P. M. (2003). Effect of a high-protein, energy restricted diet on body composition, glycemic control and lipid concentration in overweight and obese hyperinsulinemic men and women. *American Journal of Clinical Nutrition*, 78, 31-39. Retrieved from <http://ajcn.nutrition.org>
- Fonseca, V. A. (2005). The metabolic syndrome, hyperlipidemia, and insulin resistance. *Clinical Cornerstone*, 7 (2/3), 61-72. doi: 10.1016/S1098-3597(05)80069-9
- Food Standards Agency (2006). FSA Nutrient and food based guideline for UK institutions. Retrieved February 22, 2012, from <http://www.food.gov.uk/multimedia/pdfs/nutguideuk.pdf>
- Foster, G. D., Wyatt, H. R., Hill, J. O., McGuckin, B. G., Brill, C., Mohammed, S., ... Klein, S. (2003). A randomized trial of a low-carbohydrate diet for obesity. *The*

New England Journal of Medicine, 348, 2082-2090. Retrieved from <http://www.nejm.org>

- Frisch, S., Zittermann, A., Berthold, H. K., Gotting, C., Kuhn, J., Kleesiek, K., ... Kortke, H. (2009). A randomized controlled trial on the efficacy of carbohydrate-reduced or fat-reduced diets in patients attending a telemedically guided weight loss program. *Cardiovascular Diabetology*, 8, 36 1-10. doi:10.1186/1475-2840-8-36
- Gardner, C. D., Kiazand, A., Alhassan, S., Kim, S., Stafford, R. S., Balise, R. R., ... King, A.C. (2007). Comparison of the Atkins, Zone, Ornish and Learn diets for change in weight and related risk factors among overweight premenopausal women. *Journal of the American Medical Association*, 297(9), 969-977. Retrieved from <http://jama.jamanetwork.com/journal.aspx>
- Giannopoulou, I., Ploutz-Snyder, L. L., Carhart, R., Weinstock, R. S., Fernhall, B., Goulopoulou, S., & Kanaley, J. A. (2005). Exercise is required for visceral fat loss in postmenopausal women with type 2 diabetes. *The Journal of Clinical Endocrinology & Metabolism*, 90(3), 1511-1518. doi: 10.1210/jc.2004-1782
- Glenny, A-M., O'Meara, S. O., Melville, A., Sheldon, T. A., & Wilson, C. (1997). The treatment and prevention of obesity: a systematic review of the literature. *International Journal of Obesity*, 21, 715-737. Retrieved from <http://www.nature.com/ijo/index.html>
- Goldberg, G. (2003). FLAIR-FLOW 4: synthesis report on obesity for health professionals. *Nutrition Bulletin*, 28, 343-354. Retrieved from [http://onlinelibrary.wiley.com/journal/10.1111/\(ISSN\)1467-3010](http://onlinelibrary.wiley.com/journal/10.1111/(ISSN)1467-3010)
- Gordon, E. S., Goldberg, & M., Chosy, G. J. (1963). A new concept in the treatment of Obesity, *Journal of the American Medical Association*, 186, (1), pp 156-166. Retrieved February 9, 2012, from http://www.subdude-site.com/WebPages_Local/Blog/topics/health/health_atkins_lowcarb_JAMApaper_1963oct.htm
- Goris, A. H. C., Westerterp-Plantenga, M. S., & Westerterp, K. R. (2000). Undereating and underreporting of habitual food intake in obese men: selective underreporting of fat intake. *American Journal of Clinical Nutrition*, 71, 130-134. Retrieved from <http://ajcn.nutrition.org>
- Green, S. (2005). Systematic reviews and meta-analysis. *Singapore Medical Journal*, 46(6), 270-274. Retrieved from <http://smj.sma.org.sg>
- Hart, A. (2003). What is the research question? A case study in the early stages of design of a randomised controlled trial for a complementary therapy. *Complementary Therapies in Medicine*, 11, 42-45. Retrieved from <http://www.complementarytherapiesinmedicine.com>

- Healy, A. M., & Schwartz, F. L. (2010). The role of socioeconomic stress in the risk for obesity and diabetes: potential new targets of treatment. *Osteopathic Family Physician*, 2, 180-186. doi:10.1016/j.osfp.2010.08.001
- Heller, R. F., & Heller, R. F. (1991). *The carbohydrate addict's diet*. London, United Kingdom: Vermilion.
- Heller, R. F., & Heller, R. F. (1994). Hyperinsulinemic obesity and carbohydrate addiction: the missing link is the carbohydrate frequency factor. *Medical Hypothesis*, 42, 307-312. Retrieved from <http://www.medical-hypotheses.com>
- Hession, M., Rolland, C., Kulkarni, U., Wise, A., & Broom, J. (2009). Systematic review of randomized controlled trials of low-carbohydrate vs. low-fat/low/calorie diets in the management of obesity and its comorbidities. *Obesity Reviews*, 10(1), 36-50. doi: 10.1111/j.1467-789X.2008.00518.x
- Hite, A. H., Feinman, R. D., Guzman, G. E., Satin, M., Schoenfeld, R. D., & Wood, R. J. (2010). In the face of contradictory evidence: Report of the Dietary Guidelines for Americans Committee. *Nutrition*, 26, 915-924. doi:10.1016/j.nut.08.012
- Horgen, K. B., & Brownell, K. D. (2004). Confronting the toxic environment: environmental and public health actions in a world crisis. In T. A. Wadden & A. J. Stunkard (Eds.), *Handbook of obesity treatment* (pp. 95-106). New York, NY: The Guilford Press.
- Howard, B. V., & Wylie-Rosett, J. (2002). Sugar and cardiovascular disease: a statement for healthcare professionals from the Committee on Nutrition of the Council on Nutrition, Physical Activity and Metabolism of the American Heart Association. *Circulation*, 106, 523-527. doi:10.1161/01.CIR.000019552.77778.04
- Jadad, A. R., 1998. *Randomised Controlled Trials*. London, United Kingdom: BMJ Books.
- Jadad, A. R., Moore, A., Carroll, D., Jenkinson, C., Reynolds, J. M., Gavaghan, D. J., & McQuay, H. J. (1996). Assessing the quality of reports of randomized clinical trials: Is blinding necessary? *Controlled Clinical Trials*, 17, 1-12. Retrieved from <http://www.journals.elsevierhealth.com/periodicals/cct>
- James, W. P. T. (2008). The epidemiology of obesity: the size of the problem. *Journal of Internal Medicine*, 263, 336-352. doi:10.1111/j.1365-2796.2008.01922.x
- Jew, S., AbuMweis, S. S., & Jones, P. J. H. (2009). Evolution of the human diet: linking our ancestral diet to modern functional foods as a means of chronic disease prevention. *Journal of Medicinal Food*, 12(5), 925-934. doi: 10.1089/jmf.2008.0268

- Johnston, C. S., Tjonn, S. L., & Swan, P. D. (2004). High-protein, low-fat diets are effective for weight loss and favourably alter biomarkers in healthy adults. *The Journal of Nutrition*, 134, 586-591. Retrieved from <http://jn.nutrition.org>
- Johnston, C. S., Tjonn, S. L., Swan, P. D., White, A., Hutchins, H., & Sears, B. (2006). Ketogenic low-carbohydrate diets have no metabolic advantage over nonketogenic low-carbohydrate diets. *American Journal of Clinical Nutrition*, 83, 1055-1061. Retrieved from <http://ajcn.nutrition.org>
- Johnstone, A. M., Horgan, G. W., Murison, S. D., Bremner, D. M., & Lobley, G. E. (2008). Effects of a high-protein ketogenic diet on hunger, appetite and weight loss in obese men feeding ad libitum. *American Journal of Clinical Nutrition*, 87, 44-55. Retrieved from <http://ajcn.nutrition.org>
- Kauffman, J. M. (2004). Low-carbohydrate diets. *Journal of Scientific Exploration*, 18(1), 83-134. Retrieved from <http://www.scientificexploration.org/journal>
- Klem, M. L., Wing, R. R., McGuire, M. T., Seagle, H. M., & O Hill, J. (1997). A descriptive study of individuals successful at long-term maintenance of substantial weight loss. *American Journal of Clinical Nutrition*, 66, 239-246. Retrieved from <http://ajcn.nutrition.org>
- Kumar, R. (1999). *Research Methodology*. London, United Kingdom: Sage Publications.
- La Berge, A. F. (2008). How the ideology of low fat conquered America. *Journal of the History of Medicine and Allied Sciences*, 63 (2), 139-177. doi:10.1093/jhmas/jrn001
- Lara-Castro, C., & Garvey, W. T. (2004). Diet, insulin resistance, and obesity: zoning in on Data for Atkins dieters living in South Beach. *Journal of Clinical Endocrinology & Metabolism*, 89 (9), 4197-4205. doi:10.1210/jc.2004-0683
- Layman, D. K., Evans, E., Baum, J. I., Seyler, J., Erickson, D. J., & Boileau, R. A. (2005). Dietary protein and exercise have additive effects on body composition during weight loss in adult women. *Journal of Nutrition*, 135, 1903-1910. Retrieved from <http://jn.nutrition.org>
- Leidy, H. J., Carnell, N. S., Mattes, R. D., & Campbell, W. W., (2007). Higher protein intake preserves lean mass and satiety with weight loss in pre-obese and obese women. *Obesity* 15, (2), 421-429. Retrieved from <http://www.nature.com/oby/index.html>
- Leidy, H. J., Mattes, R. D., & Campbell, W. W. (2007). Effects of acute and chronic protein intake on metabolism, appetite and ghrelin during weight loss. *Obesity*, 15, 1215-1225. Retrieved from <http://www.nature.com/oby/index.html>
- Lichtenstein, A. H., & Van Horn, L. (1998). Very low fat diets. *Circulation*, 98, 935-939. doi: 10.1161/01.CIR.98.9.935

- Lichtman, S. W., Pisarka, K., Berman, E. R., Pestone, M., Dowling, H., Offenbacher, E., ... Heymsfield, S. B. (1992). Discrepancy between self-reported and actual caloric intake and exercise in obese subjects. *The New England Journal of Medicine*, 327, 1893-1898. Retrieved from <http://www.nejm.org>
- Liese, A. D., Schulz, M., Fang, F., Wolever, T. M. S., D'Agostino, Jr., R. B., Sparks, K. C., ... Mayer-Davis, E. J. (2005). Dietary glycemic index and glycemic load, carbohydrate and fiber intake, and measures of insulin sensitivity, secretion, and adiposity in the insulin resistance atherosclerosis study. *Diabetes Care*, 28, (12), 2832-2838. Retrieved from <http://care.diabetesjournals.org>
- Luscombe-Marsh, N. D., Noakes, M., Wittert, G. A., Keogh, J. B., Foster, P., & Clifton, P. M. (2005). Carbohydrate-restricted diets high in either monounsaturated fat or protein are equally effective at promoting fat loss and improving blood lipids. *American Journal of Clinical Nutrition*, 81, 762-772. Retrieved from <http://ajcn.nutrition.org>
- Maki, K. C., Rains, T. M., Kaden, V. N., Raneri, K. R., & Davidson, M. H. (2007). Effects of a reduced-glycemic-load diet on body weight, body composition, and cardiovascular disease markers in overweight and obese adults. *American Journal of Clinical Nutrition*, 85, 724-734. Retrieved from <http://ajcn.nutrition.org>
- McAuley, K. A., Hopkins, C. M., Smith, K. J., McLay, R. T., Williams, S. M., Taylor, R. W., & Mann, J. I. (2004). Comparison of high-fat and high-protein diets with a high-carbohydrate diet in insulin-resistant obese women. *Diabetologia*, 48, 8-16. doi: 10.1007/s00125-004-1603-4
- McMillan Price, J., & Brand-Miller, J (2004). Dietary approaches to overweight and obesity. *Clinics in Dermatology*, 22, 310-314. doi:10.1016/j.clindermatol.2004.01.010
- Meckling, K. A., O'Sullivan, C., & Saari, D. (2004). Comparison of a low-fat diet to a low-carbohydrate diet on weight loss, body composition, and risk factors for diabetes and cardiovascular disease in free-living, overweight men and women. *The Journal of Clinical Endocrinology & Metabolism*, 89 (6), 2717-2723. doi:10.1210/jc.2003-031606
- MyGenomics (2012). A revolutionary nutrigenetic approach to weight management. Retrieved May 31, 2012 from <https://www.mygenomics.co.uk/site/what-Is-Your-Diet-Genotype>
- National Institute for Clinical Excellence [NICE] (2006). NICE clinical guidance 43. Obesity-Guidance on the prevention, identification, assessment and management of overweight and obesity in adults and children. Retrieved from <http://www.nice.org.uk/nicemedia/pdf/CG43NICEGuideline.pdf>

- Nordmann, A. J., Nordmann, A., Briel, M., Keller, U., Yancy, W. S., Brehm, B. J., & Bucher, H.C. (2006). Effects of low-carbohydrate vs. low-fat diets on weight loss and cardiovascular risk factors. *Archives of Internal Medicine*, 166, 285-293. Retrieved from <http://archinte.jamanetwork.com/journal.aspx>
- Parker, B., Noakes, M., Luscombe, N., & Clifton, P. (2002). Effect of a high-protein, high-monounsaturated fat weight loss diet on glycemic control and lipid levels in type 2 diabetes. *Diabetes Care*, 25, 424-430. Retrieved from <http://care.diabetesjournals.org>
- Patel, S. R., & Hu, F. B. (2008). Short sleep duration and weight gain: a systematic review. *Obesity*, 16, (3), 643-653. Retrieved from <http://www.nature.com/oby/index.html>
- Pennington, A. W. (1953a). An alternate approach to the problem of obesity. *American Journal of Clinical Nutrition*, 1(2), 100-106. Retrieved from <http://ajcn.nutrition.org>
- Pennington, A. W. (1953b). Treatment of obesity with calorically unrestricted diets. *American Journal of Clinical Nutrition*, 1(5), 343-348. Retrieved from <http://ajcn.nutrition.org>
- Pirozzo, S., Summerbell, C., Cameron, C., & Glasziou, P. (2003). Should we recommend low-fat diets for obesity? *Obesity Reviews*, 4, 83-90. Retrieved from [http://onlinelibrary.wiley.com/journal/10.1111/\(ISSN\)1467-789X](http://onlinelibrary.wiley.com/journal/10.1111/(ISSN)1467-789X)
- Reaven, G. M. (2005). The insulin resistance syndrome: definition and dietary approaches to treatment. *Annual Review of Nutrition*, 25, 17.1-17.16. doi: 10.1146/annurev.nutr.24.012003.132155
- Reaven, G. M. (2006). The metabolic syndrome: is this diagnosis necessary? *American Journal of Clinical Nutrition*, 83, 1237-47. Retrieved from <http://ajcn.nutrition.org>
- Roberts, C. K., Barnard, R. J., & Croymans, D. M. (2008). Weight loss with a low-carbohydrate, Mediterranean, or low-fat diet. *New England Journal of Medicine*, 359 (20), 2169-2172. Retrieved from <http://www.nejm.org>
- Sacks, F. M., Bray, G. A., Carey, V. J., Smith, S. R., Ryan, D. H., Anton, S. D., ... Williamson, D. A. (2009). Comparison of weight-loss diets with different compositions of fat, protein, and carbohydrates. *New England Journal of Medicine*, 360, 859-873. Retrieved from <http://www.nejm.org>
- Saltzman, E., Thomason, P., & Roberts, S. B. (2001). Fad diets: a review for the primary care provider. *Nutrition in Clinical Care*, 4 (5), 235-242. Retrieved from [http://onlinelibrary.wiley.com/journal/10.1111/\(ISSN\)1523-5408](http://onlinelibrary.wiley.com/journal/10.1111/(ISSN)1523-5408)

- Samaha, F. F., Iqbal, N., Seshadri, P., Chicano, K. L., Daily, D. A., McGrory, J., ... Stern, L. (2003). A low-carbohydrate as compared with a low-fat diet in severe obesity. *New England Journal of Medicine*, 348, 2074-2081. Retrieved from <http://www.nejm.org>
- Schwartz, M. B., & Brownell, K. D. (2007). Actions necessary to prevent childhood obesity. Creating the climate for change. *The Journal of Law, Medicine & Ethics*, 35 (1), 78-89. Retrieved from [http://onlinelibrary.wiley.com/journal/10.1111/\(ISSN\)1748-720X](http://onlinelibrary.wiley.com/journal/10.1111/(ISSN)1748-720X)
- Sears, B. & Lawren, B. (1995). *Enter the Zone*. New York, NY: HarperCollins.
- Shai, I., Schwarzfuchs, D., Henkin, Y., Shahar, D. R., Witkow, S., Greenberg, I., ... Stampfer, M. D. (2008). Weight loss with a low-carbohydrate, Mediterranean or low-fat diet. *The New England Journal of Medicine*, 359, 229-241. Retrieved from <http://www.nejm.org>
- Sharman, M. J., Gomez, A. L., Kraemer, W. J., & Volek, J. S. (2004). Very low-carbohydrate and low-fat diets affect fasting lipids and postprandial lipemia differently in overweight men. *The Journal of Nutrition*, 134, 880-885. Retrieved from <http://jn.nutrition.org>
- Siri-Tarino, P. W., Sun, Q., Hu, F. B., & Krauss, R. M. (2010). Saturated fat, carbohydrate and cardiovascular disease. *American Journal of Clinical Nutrition*, 91, 502-509. doi: 10.3945/ajcn.2008.26285
- Skidmore, P. (2007). Macronutrient intakes and their role in obesity. *Nutrition Bulletin*, 32 (supplement 1), 4-13. Retrieved from [http://onlinelibrary.wiley.com/journal/10.1111/\(ISSN\)1467-3010](http://onlinelibrary.wiley.com/journal/10.1111/(ISSN)1467-3010)
- Skov, A. R., Toubro, S., Ronn, B., Holm, L., & Astrup, A. (1999). Randomized trial on protein vs carbohydrate in ad libitum fat reduced diet for the treatment of obesity. *International Journal of Obesity*, 23, 528-536. Retrieved from <http://www.nature.com/ijo/index.html>
- Slentz, C. A., Aiken, L. B., Houmard, J. A., Bales, C. W., Johnson, J. L., Tanner, C. J., ... Kraus, W. E. (2005). Inactivity, exercise, and visceral fat. STRRIDE: a randomized, controlled study of exercise intensity and amount. *Journal of Applied Physiology*, 99, 1613-1618. doi:10.1152/jappphysiol.00124.2005
- Spiegel, K., Leproult, R., L'Hermite-Baleriaux, M., Copinschi, G., Penev, P. D., & Van Cauter, E. (2004). Leptin levels are dependent on sleep duration: Relationships with sympathovagal balance, carbohydrate regulation, cortisol, and thyrotropin. *Journal of Clinical Endocrinology & Metabolism*, 89 (11), 5762-5771. doi: 10.1210/jc.2004-1003
- Stein, C.J., & Colditz, G. A. (2004). The epidemic of obesity. *The Journal of Clinical Endocrinology & Metabolism*, 89 (6), 2522-2525. doi: 10.1210/jc.2004-0288

- Stern, L., Iqbal, N., Seshadri, P., Chicano, K. L., Daily, D. A., McGrory, J., ... Samaha, F. F. (2004). The effects of low-carbohydrate versus conventional weight loss diets in severely obese adults: one-year follow-up of a randomized trial. *Annals of Internal Medicine*, 140, 778-785. Retrieved from <http://annals.org/journal.aspx>
- Taubes, G. (2011). *Why we get fat and what to do about it*. New York, NY: Anchor Books.
- US Department of Agriculture [USDA] (2010). Dietary guidelines for Americans, 2010. (Executive Summary). Retrieved June 16, 2012, from <http://www.cnpp.usda.gov/Publications/DietaryGuidelines/2010/PolicyDoc/ExecSummary.pdf>
- Volek, J. S., Phinney, S. D., Forsythe, C. E., Quann, E. E., Wood, R. J., Puglisi, M. J., ... Feinman, R. D. (2009). Carbohydrate restriction has a more favourable impact on the metabolic syndrome than a low fat diet. *Lipids*, 44, 297-309. doi: 10.1007/s11745-008-3274-2
- Westman, E. C., Feinman, R. D., Mavropoulos, J. C., Vernon, M. C., Volek, J. S., Wortman, J. A., ... Phinney, S. D. (2007). Low-carbohydrate nutrition and metabolism. *American Journal of Clinical Nutrition*, 86, 276-284. Retrieved from <http://ajcn.nutrition.org>
- Westman, E. C., Mavropoulos, J., Yancy, W. S., & Volek, J. S. (2003). A review of low-carbohydrate ketogenic diets. *Current Atherosclerosis Reports*, 5, 476-483. Retrieved from <http://www.springer.com/medicine/cardiology/journal/11883>
- Wing, R. R., & O Hill, J. (2001). Successful weight loss maintenance. *Annual Review of Nutrition*, 21, 323-41. Retrieved from <http://www.annualreviews.org/journal/nutr>
- Wing, R. R., & Phelan, S. (2005). Long-term weight loss maintenance. *American Journal of Clinical Nutrition*, 82, 222S-225S. Retrieved from <http://ajcn.nutrition.org>
- Yancy Jr, W. S., Olsen, M. K., Guyton, J. R., Bakst, R. P., & Westman, E. C. (2004). A low-carbohydrate, ketogenic diet versus a low-fat diet to treat obesity and hyperlipidemia. *Annals of Internal Medicine*, 140, 767-777. Retrieved from <http://annals.org/journal.aspx>

APPENDIX A1: INSTRUMENT FOR DATA COLLECTION AND ANALYSIS – CRITERIA Basis of Data Collection Sheets for Selected Trials - Appendices A2 to A15

(Compiled by reference to 1) Crombie, 1996; 2) Jadad et al., 1996; 3) Downs and Black, 1998; 4) Kumar, 1999, p. 125; 5) Bowling 2002, p.137)

Criteria	Reference
Aims and objectives of the studies and reasons for undertaking the study and perceived general importance clear.	1,2,3,5
Hypothesis and research questions clearly stated	5
Dependent and independent variables identified	5
Study design and interventions clearly described, Appropriateness of the intervention	2,3,5
Study described as randomised and double blind	1,2,3
Characteristics of patients included clearly described?	3
At least one control or comparison group	2
Statistical power to detect type I and II errors discussed. Sample size justified?	1,2,3,5
Relevance to the research question being explored. Relevance to researcher.	1
Internal and External validity and reliability discussed	3,4,5
The study settings, study populations, subject inclusion and exclusion criteria	2,5
Selection, funding and information bias	1,3, 4,5
Ethical considerations, Conflict of interest discussed	5
Analysis- treatment groups comparable at baseline, basic data adequately described	1
Confounding factors described	3,5
Methodology and statistical methods described	1,5
Baseline, process and outcome measures	1, 2
Outcomes, endpoints clinically relevant and clearly described?	1,3
Description of withdrawals and drop outs? All subjects accounted for?	1,2,3
Adverse Effects and safety discussed?	1,2,3
Statistics appropriate and adequate?	2,3,5
Results clear and adequately reported	1,5
Conclusions clearly stated?	5
Generalizability and practical consequences of results?	3,5
Limitations of research and design presented	5
Future Implications discussed	5

APPENDIX A2: Data Collection Sheets - Dansinger et al. 2005

(Text and/or data extracted verbatim from study article for many of the descriptive sections. Figure, Table and Numerical references included in brackets refer to the original article).

Author	Dansinger, Gleason, Griffith, Selker & Schaefer (2005)
Title	Comparison of the Atkins, Ornish, Weight Watchers and Zone Diets for Weight Loss and Heart Disease Reduction
Journal	Journal of the American Medical Association
Quality of Journal and competence of Researchers	Peer Reviewed Journal. Reputable Key Author. Dansinger is an MD but promotes himself as a low-carb doctor- hence potential author bias. Dansinger and Schaefer are MDs and affiliated to the Division of Endocrinology, Diabetes and Metabolism and Drs Griffith and Selker are affiliated to the Institute for clinical research and health policy studies. Dr Schaefer and Ms Gleason affiliated to the Jean Mayer US Department of Agriculture Human Nutrition Centre on Aging at Tufts University.
General Aim Clear	Evaluation of four named diets for weight loss and heart disease reduction. Aim to determine their relative realistic clinical effectiveness and sustainability for weight loss and cardiac risk factor reduction.
Specific Study objectives stated	To assess adherence rates and effectiveness of 4 popular diets for weight loss and cardiac risk factor reduction.
Aim and study objectives relevant to research question being explored External Validity - relevance of this particular piece of work to the issue under scrutiny	Relevant to primary research question as to whether the macronutrient composition of a diet is significant to weight management and cardiovascular disease (CVD) risk management. Two of the four diet intervention arms lowered carbohydrates. The four diets studied were a low-carbohydrate Atkins Diet, a moderate carbohydrate Zone Diet, a low-calorie Weight Watchers diet and a very low-fat Ornish Diet.
Internal Validity - methods and actual results in the light of study objectives	Not Controlled. Comparative Intervention
Study described as randomised	Yes. 160 participants were randomly assigned to either Atkins(carbohydrate (CHO) restriction), n=40; Zone (macronutrient balance, n=40; Weight Watchers (calorie restriction, n=40; Ornish (fat restriction, n=40)
Study described as double blind	No.
Description of withdrawals and dropouts present	Yes. Completers were: Atkins: 53% (21 of 40); Zone: 65% (26 of 40; Weight Watchers: 26 of 40 (65%); Ornish: 50% (20 of 40). Participants who did not complete the study at months 2, 6, and 12 were 34 (21%), 61(38%) and 67 (42%). Reasons of dropouts and non completion provided. These included "disliked diet", "Unable to adhere", and "moved away".
Randomisation / blinding appropriate	Randomisation was relevant. Blinding for participants would not be possible as these are popular diets that participants would most likely be aware of.

APPENDIX A2: Data Collection Sheets - Dansinger et al. 2005

(Text and/or data extracted verbatim from study article for many of the descriptive sections. Figure, Table and Numerical references included in brackets refer to the original article).

Randomisation / blinding appropriate contd.	Study personnel were blinded to dietary assignment to avoid the possibility of biased recruiting according to diet type or biased dietary assessment.
Target Population	Adults of any age who were overweight or obese with BMI between 27 and 42
Why was study done? What was perceived general importance?	To address the scarcity of data addressing the health effects of popular diets especially as some of these are departing substantially from mainstream medical advice.
Is there a clear hypothesis and objectives?	Null Hypothesis – No change from baseline
What specific question is being addressed?	Are these diets effective for weight loss and for reducing cardio-metabolic risk and what is the level of adherence
The study setting- where did study take place?	At a single-centre academic medical centre in Boston Massachusetts, USA.
The study population - Intended group to whom results should apply vs. group actually studied	Overweight or obese adults with evidence of elements of cardio- metabolic disease.
Group actually studied	160 participants from the Boston Massachusetts area recruited from 247 individuals who agreed to be screened.
The social, cultural, economic, ethnic background	Individuals able to respond to newspaper advertisements, television publicity for local news coverage. Ethnic background was not disclosed but authors suggest that recruitment strategy was designed to meet race and sex criteria consistent with US federal guidelines. Demographics information is available for each group in terms of % of women, and % of white race individuals
Study Approval	Study conducted at Tufts University Academic Medical Centre. The protocol was approved by the local institutional board.
Was there clear inclusion and exclusion criteria and explanations of patient drop out? Was there clear inclusion and exclusion criteria and explanations of patient drop out? contd.	Clear inclusion criteria. Adults of any age who were overweight or obese with a BMI between 27 and 42 kg/m ² and having at least one of following metabolic cardiac risk factors: Fasting glucose of at least 110mg/dL (≥ 6.1 mmol/L); total cholesterol (TC) of at least 200mg/dL (≥ 5.2 mmol), low density lipoprotein (LDL) cholesterol of at least 130mg/dL (≥ 3.4 mmol/L); high density lipoprotein (HDL) of 40mg/dl or less (≤ 1.0 mmol/L); triglycerides of at least 150mg/dL; systolic blood pressure of at least ; 145mm Hg; diastolic blood pressure of at least 90 mm Hg or current use of oral medication to treat hypertension, type 2 diabetes or dyslipidemia Exclusion criteria-included unstable chronic illness, insulin therapy, urinary microalbumin of more than of more than 2 times normal; serum creatinine of at least 1.4 mg/dL (≥ 123.8 μ mol/L, clinically significant abnormalities of liver or thyroid test results; weight loss medication or pregnancy

APPENDIX A2: Data Collection Sheets - Dansinger et al. 2005

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Is there a power calculation to determine sample size?	Yes. Using <i>t</i> tests and 2-sided type 1 error of 5%- estimate that 40 participants needed in each group to achieve 80% power to detect a weight change of 2% from base line or 3% between diets.
Was there selection bias?	None evident. Participants recruited using newspaper advertisements and television publicity. 247 individuals screened and 160 finally selected.
Was there funding bias?	None evident. The study was supported by grants related to the National Institutes of Health (NIH).
Confounding Factors	Study only evaluated dietary components. Did not consider other specific components that may affect results. Effects of Medication cannot be quantified and separated from the effects of the dietary change. Hence the changes in metabolic markers are not purely due to dietary adjustments. Missing data analysis
How does the study group relate to researchers interest groups / patients?	The researcher's interest groups would potentially include overweight and/or obese adults with one or several of the named metabolic disorders and potentially on one or more of the related medications.
What was the intervention and how was it carried out?	4 groups were given four 1 hour sessions during first 2 months by team of a dietician and a physician. 1 st meeting group given diet, rationale, written materials and official cook book. Subsequent meetings aimed to maximize adherence by reinforcing positive dietary changes and addressing barriers to adherence. Atkins Group: aimed for less than 20g of CHO daily with a gradual increase towards 50 g daily Zone Group: aimed for 40:30:30 balance of percentage calories from CHO, fat and protein respectively Weight Watchers group aimed to keep total daily "points" in range determined by current weight. Each point was roughly 50 calories and most participants aimed for 24 to 32 points The Ornish group aimed for a vegetarian diet with 10% of calories from fat. Standardised recommendations relating to supplements, exercise and external support. All participants encouraged to take a multivitamin daily and obtain 60 minutes of exercise weekly To approximate realistic sustainability, participants asked to follow assigned diet strictly for 2 months following which they were encouraged to follow assigned diet according to self determined interest level
What was measured and how was it measured?	Dietary Adherence: Measured via participant completed 3-day food records at baseline, 1,2,6 and 12 months which were analysed via a computerized diet analysis program and a 10 point score to reflect the degree to which the group achieved the specified dietary target. Also telephoned participants monthly to rate adherence during previous 30 days.
Were baseline measures used?	Age, sex, race, smoker- more than 1 cigarette per week, hyperglycaemia – fasting blood glucose of 110mg/dL; exercise – greater than mild; mean and SD of BMI, Body weight (kg), waist size (cm); BP-systolic and diastolic in mm Hg; Glucose, Insulin,cholesterol-total, LDL, HDL, Total/HDL ratio, LDL/ HDL, triglycerides, C-reactive protein, total protein, nitrogen, creatinine levels

APPENDIX A2: Data Collection Sheets - Dansinger et al. 2005

(Text and/or data extracted verbatim from study article for many of the descriptive sections. Figure, Table and Numerical references included in brackets refer to the original article).

Were baseline measures used? Contd.	Mean total energy intake was 2059 calories with 46.4%, 34.5% and 17.6% calories derived from CHO, Fat and protein respectively. No significant caloric and macronutrient differences between groups at baseline.
Were process measures used? Were process measures used? contd.	Statistical Analysis: Analysis of variance used to assess differences in baseline variables between diet groups; independent <i>t</i> tests were used to compare baseline variables between study participants who discontinued study with those who remained. 1 sample <i>t</i> test for normally distributed variables (absolute changes for weight loss and cardiac risk variables) and Wilcoxon rank sum test for skewed variables (dietary variables) Missing data replaced by baseline data for a primary intent to treat analysis or excluded for a secondary completers analysis Pearson correlation coefficient used to compare adherence data from diet records and self reports – using a single analysis that paired the 2 mean scores for each diet across 5 time points Linear regression used to assess the relationship between changes in weight, dietary adherence variables and cardiac risk factors and to assess the independent effects of potentially confounding variables including baseline characteristics and changes in exercise and medication use P values were 2 – sided and $P \leq 0.05$ was considered statistically significant.
Were outcome measures identified? Are there clear validated outcomes?	Yes
Are the methods quantitative or qualitative?	Quantitative and Qualitative
Safety Results	No evidence of clinically significant renal impairment in any diet group. This would be a concern for the low CHO groups.
Endpoint/ Biomarker Tested	Primary end point: mean absolute change from baseline weight at 1 year within each group and relative between groups.
Are there end points other than those reported that might be relevant and important	Apo lipoprotein a and b as a significant risk factor for CVD disease along with HDL and triglycerides would have been relevant and important.
Are the endpoints relevant to actual practice	Yes.
Dietary Intake and Adherence Results	For each group dietary adherence according to self-reports decreased progressively with time and to a similar extent in each diet group. 25% of participants in each diet group sustained a mean adherence of at least 6 of 10 regarded as a clinically meaningful adherence level. At 1 year, the mean caloric reduction from baseline were 138 for Atkins, 251 for Zone, 244 for Weight Watchers and 192 for Ornish groups ($P < 0.05$, $P = 0.7$ between diets)

APPENDIX A2: Data Collection Sheets - Dansinger et al. 2005

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Weight loss and cardio-protective mechanisms identified	Adherence to diet. Caloric deficit.
Weight Loss / Body Composition results	<p>All 4 diets resulted in modest statistically significant weight loss at 1 year with no statistically significant differences between diets. In each diet group approximately 25% of the initial participants sustained a 1 year weight loss of more than 5% and approximately 10% lost more than 10% of body weight. Weight loss was highly associated with waist size reductions for all diets (Pearson $r=0.86$ at one year; $P<0.001$) with no significant difference between diets. In women mean (SD) body weight decreased by 2.4 (5.1) kg (2.5% change from baseline) and waist size by 2.3 (4.5) cm. For the men body weight decreased by 3.3 (6.4) kg (3.1 % change from baseline) and waist size by 3.1 (5.8) cm at 1 year ($P=0.30$ for sex differences)</p> <p>No significant association between diet type and weight loss ($r=0.07$; $P=0.4$)</p> <p>Strong curvilinear association between self reported dietary adherence and weight loss ($r=0.60$; $P<0.001$). Participants in the top tertile of adherence lost 7%</p>
Ketonuria Results	None noted
Cardiac Risk Factor Results	<p>All 4 diets achieved modest though statistically significant improvements in several cardiac risk factors at 1 year. All diets reduced mean LDL cholesterol levels at 1 year though for Atkins Group the reduction was not statistically significant ($P=0.07$). All diets significantly increased mean HDL cholesterol except for Ornish Group ($P=0.6$). The LDL/HDL ratio decreased approximately 10% for each group ($P<0.05$).</p> <p>No diet programme significantly altered triglycerides, blood pressure and fasting glucose at 1 year.</p> <p>The lower CHO diets (Atkins and Zone) reduced triglycerides, diastolic BP and insulin in the short term though Atkins failed to significantly reduce mean fasting insulin levels at year 1 ($P=.26$). All diets reduced 1 year C-reactive protein levels by approximately 15-20% though reduction was not significant for the Zone Diet ($P=.09$).</p> <p>Secondary analysis which excluded missing data demonstrated larger but similar changes.</p> <p>Amount of weight loss predicted amount of improvement in several cardiac risk factors. For each diet weight loss was significantly associated with changes in total/HDL cholesterol ratio ($r= -0.36$), C-reactive protein ($r= -0.37$); and insulin levels ($r= -0.39$), regardless of diet type ($P=.48$, $P=.57$, $P=.31$)</p>
Cardiac Risk Factor Results contd.	<p>No diet significantly worsened any cardiac risk factor in association with weight loss or dietary adherence at 1 year.</p>
Endocrine markers and Hormonal Effects	<p>Improvements in blood Glucose and Insulin levels for all four diets at 2m, 6m and 12m. The lower-carbohydrate diets Atkins and Zone more likely to reduce insulin in the short term (2m) though Atkins failed to significantly reduce mean fasting insulin levels at one year.</p> <p>All the diets reduced 1-year C-reactive protein levels by approximately 15% to 20% though not significant for the Zone diet.</p>

APPENDIX A2: Data Collection Sheets - Dansinger et al. 2005

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Exercise and Medication use	<p>Exercise levels according to participant reports were modestly increased from baseline throughout the trial (all $P < 0.05$) and to a similar extent for each diet group ($P = 0.7$ between diets).</p> <p>At 1 year the numbers of participants with increased and decreased exercise levels from baseline were 11 and 2 for Atkins, 10 and 7 for Zone, 14 and 3 for weight watchers and 8 and 3 for Ornish Groups.</p> <p>The amount of weight loss was positively associated with changes in exercise level ($r = 0.27$, $P = .001$) with no significant differences between diets ($P = 0.7$)</p> <p>After accounting for dietary adherence, there was no significant association between change in exercise and change in body weight or any cardiac risk factor.</p> <p>When individuals who initiated cholesterol lowering medication were excluded from the intent to treat analysis, the reductions in LDL/HDL ratios observed with each diet remained statistically significant and associations between weight loss and lipid changes were unchanged or slightly stronger.</p>
What effect may bias have on the result?	None evident
<p>The Author's conclusions - are these justified?</p> <p>The Author's conclusions - are these justified? contd.</p>	<p>A variety of popular diets can reduce weight and CVD risk factors but only for minority who can sustain dietary adherence level. Lower adherence for Atkins and Ornish group suggest diets may be too extreme. Practical techniques required to increase dietary adherence.</p> <p>Adherence rates and clinical improvements would have been better if participants had been able to freely select from 4 diet options.</p> <p>Findings challenge idea that one type of diet is best for everybody and that alternative diets can be disregarded.</p> <p>Also findings do not support notion that very low-carbohydrate diets are better than standard diets.</p> <p>Poor sustainability and adherence rates resulted in modest weight loss and cardiac risk factor reduction for each diet group as a whole.</p> <p>Cardiac risk factor reduction was associated with weight loss regardless of diet type</p> <p>Adherence level rather than diet type was key determinant of clinical benefits</p> <p>CVD outcome studies appropriate to assess potential health effects of these diets</p> <p>More research needed to identify practical techniques to increase dietary adherence and to match individuals' food preferences, lifestyle and medical conditions.</p> <p>Findings suggest that the degree to which a patient exhibits features of the metabolic syndrome might guide the degree of carbohydrate restriction.</p>
Generalizability- the extent to which the results might apply outside the study	<p>The baseline characteristics in each of the 4 diet groups were well matched and representative of the overweight population of the US. However these may be reasonably representative of South-Asian obesity and of a treatment group relevant to the researcher.</p> <p>Women were well represented and included a higher percentage of non-whites which may be relevant to South-Asian interest group.</p>

APPENDIX A2: Data Collection Sheets - Dansinger et al. 2005

(Text and/or data extracted verbatim from study article for many of the descriptive sections. Figure, Table and Numerical references included in brackets refer to the original article).

Discussion points	<p>Higher discontinuation rates for the Atkins and Ornish Groups suggest these may have been found to be extreme. Practical techniques are needed to manage a national obesity epidemic- dietary adherence may improve if a broad spectrum of diet options are used to suit individual patient food preferences, lifestyles and CVD risk profiles. Adherence may have improved if participants had freely chosen their diets</p> <p>Findings challenge the concept that 1 type of diet is best for all or that very low CHO diets are better than standard diets</p> <p>Results support growing body of research that restriction of CHO and saturated fat have different effects on CVD profile- low CHO diets increase HDL cholesterol and more effective for short- term reduction of serum triglycerides, glucose and /or insulin; low saturated fat diets decrease LDL cholesterol. Hence clinicians can tailor level of CHO restriction.</p> <p>High- CHO/low- fat reduce or fail to increase HDL cholesterol – the significance of which in terms of CVD is unclear. Increase in HDL with low CHO/high fat diets still unclear due to lack of relevant intervention trials.</p> <p>Study design limited support beyond 2 months to reflect real-world conditions. Drawback of approach for highly adherent individuals</p>
Were study limitations discussed?	<p>A much larger sample size would be required to “a best diet”</p> <p>High rate of attrition confounds the results potentially</p> <p>The assumption that participants who discontinued the study were unchanged from the baseline is reasonable but imprecise but authors feel validity supported by 3 observations</p> <p>Study limited in ability to exclude long-term safety risks or occasional dangerous adverse effects resulting from diets though no short-term safety risks were found.</p> <p>Measurement of dietary intake and adherence relied on self-reporting and therefore subjective.</p> <p>Other limitations</p> <p>Software used to analyse diet also subject to errors</p> <p>After 2 months participants encouraged to follow their diet according to their own self determined interest level. Hence this could be a confounding factor.</p> <p>Whilst this approach was useful to estimate the real world effectiveness and sustainability of diets but downside was that it was poorly suited to determine the effects of each diet in highly adherent individuals.</p>
Future Implications discussed	<p>Individualised diet plans appropriate. More research needed to identify practical techniques to increase dietary adherence including one to match individual food preferences, lifestyles and medical conditions.</p> <p>Further CVD outcome studies required to determine clinical effects of carbohydrates and saturated fats on HDL cholesterol</p>

APPENDIX A3: Data Collection Sheets (Foster et al. 2003)

(Text and/or data extracted verbatim from study article for many of the descriptive sections. Figure, Table and Numerical references included in brackets refer to the original article).

Author	Foster et al. (2003)
Title	A Randomized trial of a Low-Carbohydrate Diet for Obesity
Journal	The New England Journal of Medicine
Quality of Journal and competence of Researchers	Peer Reviewed Journal. 5 out of 10 authors are MDs and 3 PhDs
General Aim Clear	To evaluate the efficacy of the low-carbohydrate (LC), high protein (Atkins diet).
Specific Study objectives stated	To evaluate the efficacy of the LC high-protein (Atkins diet) for weight loss and managing risk factors for coronary heart disease in obese persons.
Aim and study objectives relevant to research question being explored External Validity - relevance of this particular piece of work to the issue under scrutiny	Relevant to primary research question as to whether the macronutrient composition of a diet and particularly carbohydrate (CHO) restriction is significant to weight management and CVD risk management A low-carbohydrate Atkins type diet compared with a low-fat conventional diet over 3m, 6m and 12m.
Internal Validity - methods and actual results in the light of study objectives	Randomized Controlled Trial. Comparative Intervention. One year multicentre trial.
Study described as randomised	Yes. Subjects randomly assigned at each site with the use of a random-number generator to follow one the 2 diets.
Study described as double blind	No
Description of withdrawals and dropouts present	63 persons (43 women and 20 men) participated in the study. 49 subjects completed 3 months of the study (28 on the low CHO diet and 21 on the conventional diet; 42 completed 6 months (24 on the low CHO diet and 18 on the conventional diet); 37 subjects completed 12 months (20 on the low CHO diet and 17 on the conventional diet) The percentage of dropouts at 3, 6, and 12 months was higher for the conventional diet group (30, 40, and 43% respectively) than in the low CHO diet (15, 27 and 39%) but these differences were not statistically significant. Overall 59 % of subjects completed the study; 88% of those who completed the six month assessment completed the study.

APPENDIX A3: Data Collection Sheets (Foster et al. 2003)

(Text and/or data extracted verbatim from study article for many of the descriptive sections. Figure, Table and Numerical references included in brackets refer to the original article).

Randomisation / blinding appropriate	Subjects were randomly assigned at each site with use of a random number generator to follow either the low-carbohydrate high protein Atkins diet or a high-carbohydrate, low- fat, conventional diet.
Target Population	Obese Adults
Why was study done? What was perceived general importance?	To evaluate the effectiveness of the low-carbohydrate high protein, high fat Atkins diet on weight loss and CVD risk factors
Is there a clear hypothesis and objectives?	Not clearly stated but adequately implied.
What specific question is being addressed?	Is the low-carbohydrate Atkins diet effective and safe?
The study setting- where did study take place?	Multicenter study at the Schools of Medicine at the Universities of Pennsylvania, Colorado, Washington, St Louis & Thomas Jefferson University, Philadelphia.
Group actually studied	A total of 63 persons (43 women and 20 men) randomly assigned to follow either a low CHO, high protein, high fat Atkins diet or a high CHO, low-fat, energy deficit conventional diet.
The social, cultural, economic, ethnic background	20 men and 43 women, 76% white, 19% black 4% Hispanic, Average age 44. Average BMI 33.5
Study Approval	Protocol approved by the relevant institutional review boards of the participating institutions. All subjects provided written informed consent.
Was there clear inclusion and exclusion criteria and explanations of patient drop out?	Potential subjects excluded if they had clinically significant illnesses including type 2 diabetes, were taking lipid lowering medications, were pregnant or lactating or were on medication that may affect body weight.
Is there a power calculation to determine sample size?	Not evident.
Was there selection bias?	Unable to ascertain. None evident.
Was there funding bias?	Grants from NIH – No funding bias evident.
Confounding Factors	Daily multivitamin supplement. Did this impact on weight loss? Activity levels not measured or accounted for.

APPENDIX A3: Data Collection Sheets (Foster et al. 2003)

(Text and/or data extracted verbatim from study article for many of the descriptive sections. Figure, Table and Numerical references included in brackets refer to the original article).

How does the study group relate to researchers interest groups / patients?	Researcher's interest matches study group
What was the intervention and how was it carried out?	<p>Professional Contact was minimal to approximate the approach used by most dieters.</p> <p>All subjects completed a comprehensive medical examination and routine blood tests.</p> <p>Subjects in both groups instructed to take a daily multivitamin supplement and met with a registered dietician for 15 to 30 minutes at 3, 6, and 12 months to review dietary issues.</p> <p>33 low- CHO subjects met with a registered dietician to review the Atkins type diet which involved limiting CHO intake without restricting fat and protein. For the first 2 weeks CHO intake is limited to 20g per day and is then gradually increased till a stable desired weight is achieved.</p> <p>Each subject given a copy of Dr Atkins New Diet Revolution and instructed to read the book and follow the diet as described.</p> <p>The 30 subjects assigned to the conventional diet reviewed with a dietician the high-CHO, low-fat, low-calorie (1200 to 1500 kcal per day for women and 1500 to 1800 kcal per day for men with 60% of calories from CHO; 25% from fat and 15% from protein.</p> <p>They had to receive instruction about calorie counting.</p> <p>Subjects were given a copy of the Learn Program for Weight Management which provides 16 lessons on weight control.</p>
What was measured and how was it measured?	<p>Body weight using calibrated scales with subjects wearing light clothing and no shoes was measured at baseline, and at weeks 2, 4, 8,12,16,20,26,34,42 and 52.</p> <p>Blood pressure and urinary ketones were also assessed at baseline and at weeks 2,4,8,12,16,20,26, 34,42 & 52</p> <p>Blood samples obtained after subjects fasted overnight at baseline, 3, 6 and 12 months to determine serum lipoproteins concentrations</p> <p>An oral glucose tolerance test performed at baseline and at 3, 6, and 12 months. After overnight fasting, blood samples were obtained or measurement of plasma glucose and insulin concentrations were measured before and 30, 60, 90 and 120minutes after oral administration of a 75g glucose load.</p> <p>Insulin sensitivity assessed using the quantitative insulin-sensitivity check index</p>
Were baseline measures used?	Baseline characteristics shown in table in Paper. The 2 experimental groups were comparable with no significant differences in terms of sex distribution, age, weight, BMI, CVD and hormonal markers.
Were process measures used?	<p>LDL cholesterol concentration was calculated according to the Friedwald formula. TC, HDL and triglyceride levels were measured according to procedures recommended by the Centres for Disease Control and Prevention.</p> <p>Plasma insulin was measured by radioimmunoassay and plasma glucose by a glucose oxidase autoanalyser.</p> <p>Urinary ketone concentrations were measured with dipsticks.</p> <p>Data on all subjects at all sites were analysed together.</p> <p>A t-test for independent samples was used to assess differences in baseline variables between the groups.</p>

APPENDIX A3: Data Collection Sheets (Foster et al. 2003)

(Text and/or data extracted verbatim from study article for many of the descriptive sections. Figure, Table and Numerical references included in brackets refer to the original article).

Were process measures used? contd.	Two sets of analyses were conducted. The primary analysis was a repeated measures ANOVA in which baseline values were carried forward in the case of missing data. In a secondary analysis an analysis of covariance, in which initial weights were covariates was used to examine changes in weight from baseline to the end of the study for those who completed the study. A chi-square analysis was performed to determine differences between groups in categorical variables and correlations with categorical variables were assessed with Spearman's rho coefficient. Triglyceride values were not normally distributed so log –transformed values were analysed.
Were outcome measures identified? Are there clear validated outcomes?	Weight, Attrition, Urinary Ketones, BP, Oral Glucose tolerance test, Serum Lipoproteins.
Are the methods quantitative or qualitative?	Both quantitative and qualitative
Safety Results	Urinary Ketones The % of patients who tested positive for urinary ketones was significantly greater in the low CHO group in relation to the conventional diet group but there were no significant differences after 3 months. No significant relation between weight loss and ketosis at any time during the study The data suggests that ketosis was unlikely to be responsible for the increased weight loss with the low- CHO diet because the researchers did not find any relation between presence of urinary ketones and weight loss. Furthermore urinary ketones were not present in most subjects on either diet after first six months.
Endpoint/ Biomarker Tested	Body weight, BP, urinary ketones, serum lipoprotein concentrations, glucose tolerance, plasma glucose and insulin concentrations before and 30, 60, 90, 120 minutes after oral administration of 75g glucose load
Are there end points other than those reported that might be relevant and important	Apo lipoprotein a and b The study was focused on weight and specific risk factors for CHD. It did not evaluate effects on other important clinical end points such as renal function, bone health and exercise tolerance.
Are the endpoints relevant to actual practice	Yes and consistent with other studies
Dietary Intake and Adherence Results	Adherence and Attrition 49 subjects completed 3 months of the study (28 on the low CHO diet and 21 on the conventional diet; 42 completed 6 months (24 on the low CHO diet and 18 on the conventional diet); 37 subjects completed 12 months (20 on the low CHO diet and 17 and the conventional diet)

APPENDIX A3: Data Collection Sheets (Foster et al. 2003)

(Text and/or data extracted verbatim from study article for many of the descriptive sections. Figure, Table and Numerical references included in brackets refer to the original article).

Dietary Intake and Adherence Results. contd.	<p>The percentage of dropouts at 3, 6, and 12 months was higher for the conventional diet group (30, 40, and 43% respectively) than in the low CHO diet (15, 27 and 39%) but these differences were not statistically significant.</p> <p>Overall 59 % of subjects completed the study; 88% of those who completed the six month assessment completed the study.</p>
Weight loss and cardioprotective mechanisms identified	<p>The difference in weight loss between the two groups in the first six months demonstrates an overall greater energy deficit in the low-carbohydrate group, despite unrestricted protein and fat intake in this group and instructions to restrict energy intake in the conventional-diet group.</p> <p>The mechanism responsible for the decreased energy intake induced by a low-carbohydrate diet with unrestricted protein and fat intake is not known but may be related to the monotony or simplicity of the diet, alterations in plasma or central satiety factors, or other factors that affect appetite and dietary adherence.</p> <p>Data suggests that ketosis was unlikely to be responsible for the increased weight loss with the low-carbohydrate diet, since we did not find any relation between the presence of urinary ketones and weight loss. Furthermore, urinary ketones were not present in most subjects on either diet after the first six months.</p>
Weight Loss / Body Composition results	<p>In the analysis in which missing values were carried forward, the group on the low-CHO diet lost significantly more weight than the conventional diet group at 3months (P=0.001) and at 6 months (P=0.02) but the difference was not statistically significant at 12 months (P=0.26).</p> <p>Subjects on the low-carbohydrate diet had lost more weight than subjects on the conventional diet at 3 months (mean [\pmSD], -6.8\pm5.0 vs. -2.7\pm3.7 percent of body weight; P=0.001) and 6 months (-7.0\pm6.5 vs. -3.2\pm5.6 percent of body weight, P=0.02), but the difference at 12 months was not significant (-4.4\pm6.7 vs. -2.5\pm6.3 percent of bodyweight, P=0.26).</p>
Cardiac Risk Factor Results	<p>Systolic BP did not change significantly in either group. Diastolic BP decreased in both groups but there were no significant differences between the groups.</p> <p>No significant differences between the groups in the total or LDL cholesterol concentration except at month 3 when values were lower in the conventional diet group.</p> <p>The relative increase in HDL cholesterol and relative decrease in triglyceride concentrations was greater in the group on the low CHO diet than in the conventional diet throughout the study.</p> <p>The results of the analyses that included data on subjects who completed the study and data obtained at the time of the last follow-up visit for those who did not complete the study (Table 3 in paper) were nearly identical to the analyses in which base-line values were carried forward in the case of missing data (Table 2 in paper) with respect to blood pressure, insulin sensitivity, and serum lipoproteins.</p>

APPENDIX A3: Data Collection Sheets (Foster et al. 2003)

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Endocrine markers and Hormonal Effects	<p>Oral glucose-tolerance test- The area under the glucose curve did not change significantly in either group throughout the study. The area under the insulin curve decreased in both groups, but there were no significant differences between groups (Tables 2 and 3). There were no significant differences between groups in insulin sensitivity (assessed by the quantitative insulin-sensitivity check index).</p> <p>Both groups had significant increases in insulin sensitivity at six months, but the values were not significantly different from base line at one year (Tables 2 and 3 in the paper).</p> <p>Although subjects with diabetes were excluded from our study, many — if not most — of our subjects, because of their obesity, were probably insulin- resistant with respect to glucose metabolism.</p> <p>Treatment with either diet was associated with an improvement in insulin sensitivity as determined by an oral glucose-tolerance test; progressively less insulin was secreted to maintain the same blood glucose concentrations.</p>
Exercise and Medication use	<p>Patients were excluded if they had any clinically significant illnesses or were taking any lipid lowering or weight related medications.</p> <p>Daily Multivitamin supplement for both groups.</p>
What effect may bias have on the result?	None Evident.
The Author's conclusions - are these justified?	<p>The results of this multicenter, randomized, controlled trial demonstrate that the low-carbohydrate, high-protein, high-fat Atkins diet produces greater weight loss (an absolute difference of approximately 4 percent) than a conventional high-carbohydrate, low-fat diet for up to six months, but that the differences do not persist at one year. The magnitude of weight loss at six months in the low-carbohydrate group approximates that achieved by standard behavioral and pharmacologic treatments. These weight losses are particularly noteworthy because the diet was implemented in a self-help format and subjects had little contact with health professionals.</p> <p>The lack of a statistically significant difference between the groups at one year is most likely due to greater weight regain in the low-carbohydrate group and the small sample size. These data suggest that long-term adherence to the low-carbohydrate Atkins diet may be difficult.</p> <p>The overall effect of the low-carbohydrate diet in comparison with a conventional diet on the risk of CHD is uncertain. At the present time there is not enough information to determine whether benefits of an Atkins type diet outweigh its potential adverse effects on the risk of CHD in obese persons.</p> <p>When the energy content of an energy-deficit diet is stable, macronutrient composition does not influence weight loss.</p>

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Generalizability- the extent to which the results might apply outside the study	A long term view of the Atkins diet for generally well overweight and obese individuals and consequences is relevant to its application outside the study. Should not be generalised to overweight or obese subjects with serious obesity related diseases such as diabetes and hypercholesterolemia as these were excluded.
Discussion points	<p>The low CHO diet produced a greater weight loss (approximately 4%) than a conventional diet for up to six months but the differences do not persist at one year.</p> <p>The magnitude of the weight loss on the low- CHO diet approximates that achieved by other behavioural and pharmacologic treatments. Significant as the diet was on a self help format.</p> <p>The lack of a statistically significant difference at one year is likely due to greater weight gain in the low CHO group and small sample size.</p> <p>Long term adherence to the low CHO may be difficult.</p> <p>Difference of weight loss in the first 6 months demonstrates an overall greater energy deficit despite unrestricted protein and fat in the low CHO group and instruction to restrict energy intake in the conventional diet group.</p> <p>When the energy content of an energy deficit diet is stable, the macronutrient composition does not influence weight loss.</p> <p>The mechanism for decreased energy intake by a low CHO diet with unrestricted protein and fat is not known but may be related to monotony or simplicity of the diet, alterations in plasma or central satiety factors or other factors that affect appetite and dietary adherence.</p> <p>The data suggests that ketosis was unlikely to be responsible for the increased weight loss with the low CHO diet because the researchers did not find any relation between presence of urinary ketones and weight loss. Furthermore urinary ketones were not present in most subjects on either diet after first six months.</p> <p>Although subjects with diabetes were excluded, most of the subjects were probably insulin resistant. Treatment with either diet improved insulin sensitivity. The data does not demonstrate an effect of macronutrient composition independent of weight loss on insulin sensitivity in obese subjects without diabetes.</p> <p>However results of metabolic studies should be interpreted with caution given the study's small sample size and one year duration. Additional studies with more precise measures of insulin sensitivity are needed to evaluate this issue better.</p> <p>Health concern of consuming unrestricted saturated fat with potential to increase LDL cholesterol – established risk factor for coronary heart disease (CHD). At 3 months LDL cholesterol increased for low-CHO group but decreased in subjects on conventional diet group so difference significant. Over the longer term LDL levels closer to baseline values and not significantly different between groups.</p> <p>Increased weight loss associated with the low CHO diet may offset the adverse effect of saturated fat intake on serum LDL.</p> <p>Weight loss associated with decreases in LDL cholesterol usually observed with moderate weight loss.</p> <p>Low CHO associated with greater decreases in serum triglycerides and increases in HDL than the conventional diet which are</p>

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Discussion points – contd.	<p>also important risk factors for CHD. The magnitude of these changes approximate that obtained with pharmacologic treatments such fibric acid derivatives and niacin.</p> <p>Changes are greater than that expected from a moderate weight loss therefore it is likely that the macronutrient composition contributed to the improvement in the HDL-triglyceride axis.</p> <p>Overall effects of a low-CHO diet versus conventional diet on CHD is uncertain. The low CHO diet improved some indicators (HDL and triglycerides) but not others (BP, Insulin sensitivity and serum LDL).</p>
Were study limitations discussed?	<p>Self- help nature of treatment which is consistent with way in which the low-CHO diet is typically used, contributed to attrition rate of 41%.</p> <p>High attrition rate underscores the difficulty of long term compliance with either diet when given without supervision.</p> <p>More comprehensive behavioural treatment would probably have decreased attrition, increased adherence and improved comparison with clinic-based treatments for obesity.</p> <p>The study was focused on weight and specific risk factors for CHD. It did not evaluate effects on other important clinical end points such as renal function, bone health, cardiovascular function and exercise tolerance.</p> <p>Also the findings should not be generalized to overweight subjects or obese subjects with serious obesity related diseases such as diabetes and hypercholesterolemia.</p>
Future Implications discussed	<p>Additional long-term studies are needed to determine whether increased HDL and decreased triglycerides have the same effect on CVD outcomes when one is consuming a diet high in saturated fat.</p> <p>Also possible that diet with high saturated fat, low fruits and vegetables and fibre with low CHO diet can independently increase CHD risk.</p> <p>Additional studies needed to evaluate safety and efficacy of low-CHO, high-protein, high-fat diets</p>

APPENDIX A4: Data Collection Sheets – Frisch et al. (2009)

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Author	Frisch et al. (2009)
Title	A randomized controlled trial on the efficacy of carbohydrate-reduced or fat-reduced diets in patients attending a telemedically guided weight loss program
Journal	Cardiovascular Diabetology
Quality of Journal and competence of Researchers	Peer Reviewed Journal
General Aim Clear	The authors investigated whether macronutrient composition of energy-restricted diets influences the efficacy of a telemedically guided weight loss program.
Specific Study objectives stated	To establish whether or not a carbohydrate-restricted telemedically guided weight loss program results in a more pronounced weight loss and influences metabolic risk markers more beneficial than a fat-restricted diet does.
Aim and study objectives relevant to research question being explored External Validity - relevance of this particular piece of work to the issue under scrutiny	Relevant to primary research question as to whether the macronutrient composition of a diet is significant to weight management and cardiovascular disease (CVD) risk management. One moderate-carbohydrate Zone type diet compared with a low-fat diet
Internal Validity - methods and actual results in the light of study objectives	Randomized, comparative intervention
Study described as randomised	Yes. Participants (n = 200) were randomly assigned by computer- generated random number lists in two equal groups: the LOGI group was assigned to a low-carbohydrate diet developed by Ludwig et al. [9] and modified by Worm[19]; the DGE group received a conventional low-fat diet according to recommendations issued by the <i>Deutsche Gesellschaft für Ernährung</i> [20].
Study described as double blind	No
Description of withdrawals and dropouts present	Of a total number of 298 persons who were initially interested in attending the study 76 persons refused to participate after a first phone screening. Additional 16 persons did not meet the inclusion criteria. For the same reason six other persons were excluded at the baseline investigation at our clinic. In total, 200 persons were thus included in our study. Of the 200 participants, 35 subjects were lost during follow-up- due to non-compliance with the weight reduction program (n = 23), personal reasons (n = 7), diagnosis of Guillain-Barré syndrome (n = 1), diagnosis of a malignancy requiring chemo preventive therapy (n = 1), and pregnancy (n = 3). The number of drop-outs did not differ between study groups (P > 0.05).

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Randomisation / blinding appropriate	Randomisation between the two diets was appropriate. Blinding was not relevant as the participants were aware of the diets they were assigned.
Target Population	Overweight subjects attending a telemedically guided weight loss programme
Why was study done? What was perceived general importance?	To assess if a carbohydrate–restricted diet results in more pronounced weight loss
Is there a clear hypothesis and objectives?	To assess whether macronutrient composition of energy- restricted diets influences the efficacy of a telemedically guided weight loss programme.
What specific question is being addressed?	Is a carbohydrate-restricted weight loss programme more effective than a low-fat diet with respect to weight loss and cardiovascular risk factors?
The study setting- where did study take place?	This study was conducted between December 2005 and November 2006 at the Heart Centre North Rhine-Westphalia, Institute for Applied Telemedicine, Bad Oeynhausen, Germany. Recruitment began in November 2005 by advertisements in local newspapers and by providing information sheets at different local health insurance offices.
Group actually studied	200 overweight subjects
The social, cultural, economic, ethnic background	German residents, 18-70 year old and a BMI > 27kg/m ² with no history of CVD, ischemia, diabetes. Pregnancy, lactation and vegetarianism were exclusion criteria.
Study Approval	All participants gave written informed consent to the study procedures, which were approved by the Ethics Committee of the Ruhr-University Bochum, Faculty of Medicine, Germany.
Was there clear inclusion and exclusion criteria and explanations of patient drop out?	The criteria for eligibility were an age of 18 to 70 years and a BMI (calculated as weight in kilograms divided by height in meters squared) > 27 kg/m ² . We excluded patients with a history of any cardiovascular symptomatology. Moreover, we excluded patients with cholelithiasis, urolithiasis, insulin dependent diabetes mellitus, and pacemaker implantation. In addition, pregnancy, lactation, and vegetarianism were exclusion criteria. Further exclusion criteria were the participation in another weight loss program and medical treatment for weight reduction.
Is there a power calculation to determine sample size?	None evident
Was there selection bias?	None evident

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Was there funding bias?	<p>This study was funded by different German health insurances and the 'Institute for Applied Telemedicine', Heart Centre NRW, Ruhr University Bochum, Bad Oeynhausen, Germany.</p> <p>Discussion point re telemedicine influencing low attrition rates may involve a funding bias.</p>
Confounding Factors	None identified
How does the study group relate to researchers interest groups / patients?	Overweight subjects are within researcher's interest group. The exclusion of vegetarians does not support the researcher's interests.
What was the intervention and how was it carried out?	<p>The target macronutrient composition in the LOGI group was less than 40% of total energy intake (% energy) from carbohydrates, more than 35% energy from fat, and 25% energy from protein [21].</p> <p>The target macronutrient composition in the DGE group was more than 55% energy from carbohydrates, less than 30% energy from fat, and 15% energy from protein.</p> <p>We instructed all participants in an ambulatory training session and delivered diet books to all participants about their respective diets [19, 22, and 23]. All participants were advised to reduce their daily energy intake by at least 500 kcal.</p> <p>At study entry, each participant received an electronic scale (TC-100, I.E.M., Stolberg, Germany, mean deviation \pm 0.2 kg with standard deviation of 0.06 kg) with added Bluetooth® technology. Weekly, the actual body weight data had to be sent to the Institute of Applied Telemedicine using a mobile phone.</p> <p>The weight reduction program consisted of weekly nutrition education and dietary counselling by phone with a nutritionist during the first six months. This regular weekly support was stopped during the second half-year. The study subjects were responsible for buying and preparing foods by themselves.</p> <p>At baseline, after six months, and after twelve months, each subject attended an outpatient medical visit where body weight and height were measured in underwear on a calibrated electronic clinical scale (model 920, SECA GmbH & co. kg., Hamburg, Germany; tolerance \pm 0.2 kg). Moreover, waist circumference was assessed by standard procedures using a 150-cm anthropometric measuring tape, and body composition by bioelectrical impedance analysis (Multifrequency Analyzer Nutrigard M, Data Input GmbH, Darmstadt, Germany).</p>
What was measured and how was it measured?	We defined the presence of a metabolic syndrome after determination of waist circumference, blood levels of triglycerides, high density lipoprotein (HDL)-cholesterol, and fasting plasma glucose, blood pressure, and respective medical treatment according to current guidelines [24].

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<p>What was measured and how was it measured? contd.</p>	<p>Blood pressure was manually determined using a cuff and stethoscope.</p> <p>Blood samples were drawn from the antecubital vein after a 12-h overnight fast.</p> <p>Medical history and medical treatment were assessed using hospital documents.</p> <p>At baseline and after 1, 3, 6, and 12 months, we assessed energy and nutrient intake (diet compliance) by the use of a 3-day validated food record [25] and the amount of daily physical activity by using a standardized, validated questionnaire [26].</p> <p>We measured serum levels of total cholesterol, high-density lipoprotein (HDL)-cholesterol, low density lipoprotein (LDL)-cholesterol, triglycerides, glucose, and fructosamine using the Architect autoanalyzer (Abbott, Wiesbaden, Germany), and glycated haemoglobin (HbA1c) using the autoanalyzer HA-8160 (Menarini Diagnostics, Berlin, Germany). We used enzyme-linked immuno assay kits to assess proinsulin (IBL, Hamburg, Germany) and adiponectin (R&D Systems GmbH, Wiesbaden-Nordenstadt, Germany). All intra- and interassay coefficients of variation were below 10.0%.</p>
<p>Were baseline measures used?</p>	<p>Characteristics at study entry were comparable between groups, with the exception of sex distribution and fat-free mass (Table 1). (Figure 1). Medication use was similar between groups at baseline (Table 1) and did not change during the study period (data not shown).</p> <p>Energy and macronutrient intake and energy expenditure are shown in Table 2. At baseline, energy intake, energy expenditure and macronutrient composition were similar in both groups.</p>
<p>Were process measures used?</p>	<p>We expressed categorical variables as percentage rates and continuous variables as mean \pm standard deviation or standard error of the mean, when appropriate. Because several variables such as fat-free mass, diastolic and systolic blood pressure, glucose, HbA1c, proinsulin, triglycerides, HDL-cholesterol, and adiponectin were not normally distributed as tested by the Kolmogorov-Smirnov test, these data were normalized using logarithmic transformation. We used the unpaired t-test to compare continuous values of the study groups at baseline. For comparative evaluations of categorical variables, we used the Chi Square test. Results of anthropometric, clinical, and biochemical parameters at the 6-month and 12-month examinations are presented as change from baseline. The unpaired t-test and the paired t-test were used to specify those time points with significant differences between groups or within groups, when appropriate.</p> <p>A 2-factor analysis of covariance was used to compare anthropometric, clinical, and biochemical parameters between the LOGI and DGE groups with its respective baseline value and with fat-free mass and sex distribution as covariates.</p> <p>Data were evaluated following the intention-to-treat and the per-protocol method. Missing data were replaced with baseline data in the intention-to-treat analysis. P values <0.05 were considered statistically significant. P values between 0.05 and 0.10 were considered borderline significant. Considering a standard deviation of 3.5 kg, the statistical power ($\alpha = 0.05$; $\beta = 0.80$) was sufficient to detect a difference in body weight of 1.3 kg between the two study groups. We used SPSS, version 14.0 (SPSS Inc., Chicago, IL), to perform the statistical analyses.</p>

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Are the methods quantitative or qualitative?	Quantitative and qualitative.
Safety Results	None reported.
Endpoint/ Biomarker Tested	Weight loss and loss of fat mass were primary endpoints. Metabolic and cardiovascular risk markers such as waist circumference, blood pressure, blood lipids, and parameters of glucose metabolism were considered secondary endpoints.
Are there end points other than those reported that might be relevant and important	Apo lipoprotein a and b
Are the endpoints relevant to actual practice	Yes relevant to actual practice.
Dietary Intake and Adherence Results	<p>During the first six months energy intake decreased by approximately 400 kcal/d compared to baseline in both groups. At month 12, mean energy intake had slightly increased again in both groups but remained below baseline values. Metabolic rate increased in both groups. Mean macronutrient composition differed significantly between both groups from month 1 to month 12. During the study period, carbohydrate intake was between 11% and 7% higher in the DGE group compared with the LOGI group. In addition, the LOGI group had a 4% to 8% higher fat intake and a 2% to 3% higher protein intake than the DGE group, whereas alcohol intake did not differ between groups (data not shown). Especially the DGE group did not achieve the target for carbohydrate intake (> 55%).</p> <p>The use of telemedicine permits continuous contact to participants, individual support, and control of weight loss. Moreover, use of this technique resulted in a low drop-out rate of only 17% in our study participants.</p>
Weight loss and cardio-protective and other mechanisms identified	<p>It has been assumed that the better 1-year efficacy of carbohydrate- restricted diets on weight loss compared to fat-restricted diets can be explained by a greater energy deficit in subjects on a low-carbohydrate intake. Since mean energy intake and energy expenditure did not differ between the two groups, the differences in the aforementioned parameters are most likely due to differences in macronutrient relations. However, despite similar energy intake at month 12, weight loss tended to be greater at month 12 in the LOGI group compared with the DGE group of our study.</p> <p>Note that differences in macronutrient composition of the diet may influence resting or postprandial energy expenditure.</p> <p>Since protein intake increases diet-induced thermogenesis, it can well be that the slightly higher protein intake in the LOGI group compared with the DGE group during the entire study period could also have resulted in a slightly higher metabolic rate, and thus in a slightly higher weight loss.</p>

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<p>Weight loss and cardio-protective and other mechanisms identified – contd.</p>	<p>Our results are in line with a very recently published trial by Sacks et al. [30]. They investigated four diets with different macronutrient relations and showed that weight loss is related to adherence and attendance to instructional sessions.</p> <p>Despite the favourable effects of both diets on weight loss in our study, the carbohydrate-reduced diet was more beneficial with respect to some cardiovascular risk markers such as waist circumference, triglycerides, HDL-cholesterol, and systolic blood pressure compared to the fat reduced diet. Our data show into the same direction than earlier study results [12-14, 29, 31, 32] but were less pronounced. This may at least in part be due to two factors: the comparably higher weight loss by carbohydrate-restricted diets in these earlier studies [12, 13, 29, 30], and/ or a more pronounced carbohydrate restriction in the low-carbohydrate diets used [12-14, 29, 31].</p> <p>Low-carbohydrate diets may diminish triglyceride production in the liver in response to decreased carbohydrate delivery [14].</p> <p>The greater preservation of HDL-cholesterol on a low-carbohydrate diet may be the result of down-regulation by dietary fats of those hepatic receptors, which bind HDL-cholesterol [33]. However, it remains unclear why HDL-cholesterol and triglycerides differed only at the 6-month visit between the two groups of our study. It may well be that the transient effects on triglycerides and HDL cholesterol are related to differences in macronutrient composition in our study groups which became smaller over time (Table 3).</p> <p>Obviously, other variables like waist circumference and systolic blood pressure were only influenced by the degree of weight loss in the two groups and not by macronutrient composition (Table 3).</p> <p>It should also be mentioned that the similar loss in body weight in both groups of our study was associated with a similar improvement in several metabolic risk markers such as fat mass, diastolic blood pressure, and glucose, fructosamine, proinsulin, and adiponectin blood concentrations (Table 3).</p> <p>Decreasing insulin resistance and increasing adiponectin levels reduces atherosclerotic and inflammatory processes and endothelial dysfunction [35- 37] and may thus have decreased the cardiovascular risk in both study groups.</p>
<p>Weight Loss / Body Composition results</p>	<p>Both diets resulted in similar weight loss (Figures 2 and 3). In detail, weight loss was 7.2 ± 5.4 kg in the LOGI group and 6.2 ± 4.8 kg in the DGE group at month 6.</p> <p>In the second half-year, mean weight regain was 1.6 kg in the LOGI group and 1.9 kg in DGE group. Thus, at the end of the study weight loss was 5.8 ± 6.1 kg in the LOGI group and 4.3 ± 5.1 kg in the DGE group at month 12, a difference that reached borderline significance ($p = 0.065$).</p> <p>In both groups, approximately 76% of weight reduction was due to a loss of fat mass.</p> <p>Waist circumference decreased in both study groups (Table 3). At month 6, values did not differ between groups. At month 12,</p>

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Weight Loss / Body Composition results contd.	however, the decrease in waist circumference was more pronounced in the LOGI group compared with the DGE group even when adjustments were made for fat-free mass, and sex distribution.
Ketonuria Results	Not applicable
Cardiac Risk Factor Results	<p>Triglyceride levels did not change from baseline to month 6 and month 12 in the DGE group, but declined in the LOGI by 14% at month 6, and 7% at month 12 compared to baseline values.</p> <p>HDL-cholesterol decreased in the DGE group until month 6, but rose again in the second half year, whereas this parameter remained unchanged in the LOGI group.</p> <p>Changes from baseline in triglyceride and HDL-cholesterol levels differed significantly between the LOGI and DGE groups at month 6. However, these differences disappeared later on in the study.</p> <p>Total-cholesterol was not affected in the LOGI-group but increased in the DGE group between month 6 and 12. Nevertheless, total cholesterol did not differ significantly between groups at any time point.</p> <p>Diastolic blood pressure decreased in both groups, whereas systolic blood pressure was significantly higher at month 12 in the DGE group compared with the LOGI group.</p> <p>The differences in systolic blood pressure at month 12 remained significant after adjustments were made for fat free mass and sex distribution.</p>
Endocrine markers and Hormonal Effects	Changes in parameters of glucose metabolism were similar between groups For the low-carb group Glucose reduced by -0.26 ± 0.76 mmol/l at 6 months and by 0.25 ± 0.75 at 12months and for the high-carb group by 0.28 ± 0.14 at 6 m and 0.14 ± 0.46 at 12months. HbA1c reduced by $0.2 \% \pm 0.2$ for both groups at 6m and 12m.
Exercise and Medication use	Energy expenditure between the two groups was similar at baseline and reasonably similar at 1 m, 3 m, 6m and 12months. Medication use at baseline provided.
What effect may bias have on the result?	None evident
The Author's conclusions - are these justified?	Despite the favourable effects of both diets on weight loss, the carbohydrate-reduced diet was more beneficial with respect to major cardiovascular risk factors such as central obesity, triglycerides, HDL-cholesterol, and systolic blood pressure compared to the fat-reduced diet. Nevertheless, compliance with a weight loss program appears to be even a more important factor for success in prevention and treatment of obesity than the composition of the diet.

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The Author's conclusions - are these justified? Contd.	Despite some additional beneficial effects of energy-restricted low-carbohydrate diets on cardiovascular risk markers it appears that poor long-term adherence to such diets limits its success in clinical practice [34]. Note reference 34 is Dansinger et al. (2005) included in this review and it is significant that supervision ceased after 2 months which could explain the lower levels of adherence.
Generalizability- the extent to which the results might apply outside the study	The results of a telemedically monitored protocol providing continuous contact with participants , individual support and control of weight loss provides an interesting technique to promote adherence and enable a lower drop-out rate.
Discussion points	<p>In this telemedically guided weight reduction program both, an energy-restricted high-carbohydrate diet (DGE group) and an energy-restricted low-carbohydrate diet (LOGI group) resulted in a satisfactory weight loss and an improvement of several metabolic parameters over a period of 12 months.</p> <p>However, weight loss tended to be greater, and the decline in waist circumference and systolic blood pressure was more pronounced in the LOGI group than in the DGE group.</p> <p>With respect to HDL-cholesterol and triglycerides, beneficial effects in the LOGI group compared to the DGE group were only seen at the 6-month follow-up visit.</p> <p>Since mean energy intake and energy expenditure did not differ between the two groups, the differences in the aforementioned parameters are most likely due to differences in macronutrient relations.</p> <p>The mean body weight loss of 7.2 kg at month 6 and 5.8 kg at month 12 in the LOGI group (Figure 3) was similar compared to literature reports about efficacy of carbohydrate- restricted diets [12-15,29]. In these earlier reports, results of carbohydrate-restricted diets were also compared with fat-restricted diets.</p> <p>Mean weight loss of the fat restricted diets was only 1.6 kg – 3.9 kg at month 6 [12- 15,29] and 2.2 kg – 3.1 kg at month 12 [12,14,29] and thus lower than the mean weight loss in the energy restricted fat-reduced group (DGE group) in our study (6.2 kg at month 6 and 4.3 kg at month 12, respectively).</p> <p>It has been assumed that the better 1-year efficacy of carbohydrate- restricted diets on weight loss compared to fat-restricted diets can be explained by a greater energy deficit in subjects on a low-carbohydrate intake.</p> <p>Since in our study energy intake and body weight loss were similar in both groups within the first 6 month, our results are in line with the aforementioned hypothesis.</p> <p>However, despite similar energy intake at month 12, weight loss tended to be greater at month 12 in the LOGI group compared with</p>

APPENDIX A4: Data Collection Sheets – Frisch et al. (2009)

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Discussion points – contd.	<p>the DGE group of our study.</p> <p>Note that differences in macronutrient composition of the diet may influence resting or postprandial energy expenditure [15].</p> <p>Since protein intake increases diet-induced thermogenesis, it can well be that the slightly higher protein intake in the LOGI group compared with the DGE group during the entire study period could also have resulted in a slightly higher metabolic rate, and thus in a slightly higher weight loss.</p> <p>Nevertheless, our data also demonstrate that even with an energy-restricted high-carbohydrate diet a weight loss similar to an energy-restricted carbohydrate-reduced diet can be achieved.</p> <p>Importantly, the regain of weight after 12 months confirms earlier assumptions [17, 18] that continuous intensive care and control is a more important factor for participants' compliance and, thus, for the success of a weight loss program than minor alterations in macronutrient composition in the diet.</p> <p>Our results are in line with a very recently published trial by Sacks et al. (2009) [30]. They investigated four diets with different in Sacks et al. macronutrient relations and showed that weight loss is related to adherence and attendance to instructional sessions. All the diets in Sacks et al. (2009) were equally successful in promoting weight loss and maintaining weight.</p> <p>Despite the favourable effects of both diets on weight loss in our study, the carbohydrate-reduced diet was more beneficial with respect to some cardiovascular risk markers such as waist circumference, triglycerides, HDL-cholesterol, and systolic blood pressure compared to the fat reduced diet. Our data show into the same direction than earlier study results [12-14, 29, 31, 32] but were less pronounced. This may at least in part be due to two factors: the comparably higher weight loss by carbohydrate-restricted diets in these earlier studies [12, 13, 29, 30], and/ or a more pronounced carbohydrate restriction in the low-carbohydrate diets used [12-14, 29, 31].</p> <p>Low-carbohydrate diets may diminish triglyceride production in the liver in response to decreased carbohydrate delivery [14].</p> <p>The greater preservation of HDL-cholesterol on a low-carbohydrate diet may be the result of down-regulation by dietary fats of those hepatic receptors, which bind HDL-cholesterol [33]. However, it remains unclear why HDL-cholesterol and triglycerides differed only at the 6-month visit between the two groups of our study. It may well be that the transient effects on triglycerides and HDLcholesterol are related to differences in macronutrient composition in our study groups which became smaller over time (Table 3).</p> <p>Obviously, other variables like waist circumference and systolic blood pressure were only influenced by the degree of weight loss in the two groups and not by macronutrient composition (Table 3).</p>
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APPENDIX A4: Data Collection Sheets – Frisch et al. (2009)

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Discussion points contd.	<p>Our results also demonstrate the general problem of adherence to a diet with extreme nutrition relations.</p> <p>The use of telemedicine permits continuous contact to participants, individual support, and control of weight loss. Moreover, use of this technique resulted in a low drop-out rate of only 17% in our study participants.</p> <p>Note that earlier investigations have already reported relatively high attrition-rates of 30–50% in studies using very low-carbohydrate diets [12, 34].</p> <p>It should also be mentioned that the similar loss in body weight in both groups of our study was associated with a similar improvement in several metabolic risk markers such as fat mass, diastolic blood pressure, and glucose, fructosamine, proinsulin, and adiponectin blood concentrations (Table 3).</p> <p>Decreasing insulin resistance and increasing adiponectin levels reduces atherosclerotic and inflammatory processes and endothelial dysfunction [35- 37] and may thus have decreased the cardiovascular risk in both study groups.</p>
Were study limitations discussed?	<p>It was not possible to achieve the target macronutrient relations in the two study groups in the long run. The target of carbohydrate content in the LOGI group (< 40% energy) was only reached within the first 3 months and the target of carbohydrate content in the DGE group (>55% energy) was not reached at any time.</p>
Future Implications discussed	<p>The use of telemedicine and /or continuous contact via the internet to monitor patients is relevant for future investigation Refer to the Dukan online support process.</p>

APPENDIX A5: Data Collection Sheets – Johnston et al. (2006)

(Text and/or data extracted verbatim from study article for many of the descriptive sections. Figure, Table and Numerical references included in brackets refer to the original article).

Author	Johnston et al. (2006)
Title	Ketogenic low-carbohydrate diets have no metabolic advantage over nonketogenic low-carbohydrate diets
Journal	American Journal of Clinical Nutrition.
Quality of Journal and competence of Researchers	Peer Reviewed Journal. Two of the authors were connected with the Zone Diet which was similar to the non ketogenic low carbohydrate diets in the study. Barry Sears is the author of the Zone diet and on the Board of Zone Labs Inc. and Heather Hutchins is an employee of Zone Labs Inc.
General Aim Clear	To assess the significance of a ketogenic low-carbohydrate weight loss diet with a less restrictive non ketogenic weight loss diet.
Specific Study objectives stated	To compare weight loss and biomarker change in adults on a ketogenic low-carbohydrate (KLC) or a non ketogenic low carbohydrate (NLC) diet.
Aim and study objectives relevant to research question being explored External Validity - relevance of this particular piece of work to the issue under scrutiny	Relevant to primary research question as to whether the macronutrient composition of a diet and particularly CHO restriction is significant to weight management and CVD risk management. Particularly relevant in assessing effects of the level of CHO consumed. Two low-carbohydrate diet arms compared. An Atkins type diet and a Zone type diet.
Internal Validity - methods and actual results in the light of study objectives	Randomized Controlled Trial. 6 week study.
Study described as randomised	Yes. Subjects were stratified by age, sex and BMI and randomly assigned to one of two diets.
Study described as double blind	No
Description of withdrawals and dropouts present	One participant in the KLC developed heart arrhythmia during the first week and was dropped from study.
Randomisation / blinding appropriate	Blinding not appropriate. Subjects were stratified by age, sex and BMI and randomly assigned to one of two diets.
Target Population	Generally well, overweight sedentary Adults between 20-60 years, screened for diagnosed disease and prescription medication.
Why was study done? What was perceived general importance?	In the context of low-carbohydrate diets for weight loss the significance of how much carbohydrate restriction is necessary to attain effective results is the key question.

APPENDIX A5: Data Collection Sheets – Johnston et al. (2006)

(Text and/or data extracted verbatim from study article for many of the descriptive sections. Figure, Table and Numerical references included in brackets refer to the original article).

Is there a clear hypothesis and objectives?	To compare a ketogenic vs. a non-ketogenic diet in the context of an energy restricted diet.
What specific question is being addressed?	Does a low-carbohydrate diet have to be ketogenic to be effective for weight loss?
The study setting- where did study take place?	Department of Nutrition , University of Arizona
The study population - Intended group to whom results should apply vs. group actually studied	20 sedentary, overweight men and women, aged 20-60y; body mass index >25.
The social, cultural, economic, ethnic background	Not much known about the social cultural or ethnic background of the subjects.
Study Approval	Study protocol approved by the Institutional Review Board of Arizona State University. All participants gave written informed consent.
Was there clear inclusion and exclusion criteria and explanations of patient drop out?	Sedentary, overweight men and women [aged 20–60 y; body mass index (BMI; in kg/m ²) _ 25] were screened for diagnosed disease and use of prescription medications. One participant (KLC diet group) developed heart arrhythmias during the first week and was dropped from the study.
Is there a power calculation to determine sample size?	Although the study was limited by the small sample size, power calculations did indicate a 70% power to detect a change of 0.6mmol/L in LDL cholesterol. Pearson's correlation was used to identify relations between variables.
Was there selection bias?	Not evident
Was there funding bias?	Barry Sears, a key author is a stockholder and serves on the boards of directors of Zone Labs Inc and other Zone companies supporting non-ketogenic diets.
Confounding Factors	None noted
How does the study group relate to researchers interest groups / patients?	Overweight subjects who may not be obese are within the clinical interest area of the researcher.
What was the intervention and how was it carried out?	Study compared weight loss and metabolic effects of a ketogenic LC diet (beginning with <20g carbohydrates) and a non ketogenic diet (40% energy as carbohydrate).

APPENDIX A5: Data Collection Sheets – Johnston et al. (2006)

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<p>What was the intervention and how was it carried out? Contd.</p>	<p>All food and drink were provided to subjects and energy intake was strictly controlled to participants who remained sedentary. All food and drink was prepared and served to participants. Hot lunches prepared and served to participants- Monday through Friday. Breakfast, dinner and weekend meals prepared and packaged for participants to take home.</p> <p>After the 6 week trial participants were instructed to continue with their allocated diet on their own for 4 weeks.</p> <p>A registered dietician discussed diet details and meal plans with each participant for these 4 weeks.</p> <p>The protein content of the 2 diets was comparable (30% of energy) but the KLC diet was high in fat (60% of energy with saturated fat 21% of energy) and very low in carbohydrates (beginning with approx 5% of energy) whereas the NLC diet was low in fat (30% of energy with saturated fat of 9%) and carbohydrates (approx 40% of energy). The carbohydrate content of the KLC was increased by 5g/wk in weeks 3-6 and this group was asked to consume 40g of CHO during the self-monitored phase of the trial.</p> <p>The NLC had $\geq 67\%$ of recommended dietary intakes (RDA) for the micronutrients; the KLC was less nutritious : fibre, Vitamin E , folate, iron, magnesium and potassium were $< 67\%$ of RDA. re provided a daily multivitamin and mineral tablet beginning at the end of week 2v of the 6 week trial.</p> <p>Diets were developed by a registered dietician using FOOD PROCESSOR for WINDOWS nutrition analysis software.</p> <p>A 14-day rotating menu was devised for each diet plan. Foods were prepared using scales and liquid measures.</p> <p>Participants within diet groups had similar meal plans but daily energy intakes were individually adjusted by altering portion size to provide approximately 70% of that needed for weight maintenance.</p>
<p>What was measured and how was it measured?</p>	<p>On day 1 of each week of 6 week trial, body weight and fat mass were recorded using a Tanita Body Composition analyser.</p> <p>A 7 point Likert scale was used to assess hunger and how they felt generally over the past week.</p> <p>A Profile of Mood States (POMS) questionnaire that assessed 6 mood states was completed.</p> <p>Body weight and fat mass were also recorded at week 10.</p> <p>Before start of trial and at weeks 2 and 6 participants provided a 24-hr urine sample; Resting Energy Expenditure (REE) was measured after a 12 hour fast a 24 hour avoidance of light to heavy activity.</p> <p>A fasting blood sample was collected at weeks 0, 2 and 6.</p>

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Were baseline measures used?	Baseline indices did not vary by group.
Were process measures used?	<p>REE was estimated from a mean of 20 minutes of continuous gas sampling via indirect calorimetry by using a prescribed formula and adjusting for body mass.</p> <p>Serum concentrations of glucose, creatinine; total, HDL and LDL cholesterol and triacylglycerols were measured at Sonora Quest Laboratories.</p> <p>Plasma Insulin was measured using radioimmunoassay and insulin sensitivity was assessed using the homeostasis model assessment (HOMA) index for insulin resistance (mmol fasting glucose/L) X μU fasting insulin /mL/22.5.</p> <p>Urinary creatinine was measured using colorimetric procedures.</p> <p>Plasma uric acid, C-reactive protein, liver enzymes and urinary calcium were also measured.</p> <p>Blood β-hydroxybutyrate was measured enzymatically by using an autoanalyser</p> <p>Fatty acid composition of isolated serum phospholipids reported as the ratio of arachidonic acid to eicosapentenoic acid was analysed by gas chromatography.</p> <p>Statistical Analyses were performed using SPSS for windows software. The repeated measures analysis of variance with main effects of time and group time interaction was used to assess differences in metabolic data.</p> <p>To assess change in body mass at week 6 by group or to ascertain whether a significant group X time interaction was observed for metabolic parameters, an unpaired Student's <i>t</i> test was performed.</p>
Were outcome measures identified? Are there clear validated outcomes?	Body Weight , Fat mass, fat free mass, hunger ratings, feelings of vigour-activity, 6 distinct mood states (tension-anxiety, depression-dejection, anger-hostility, vigour-activity, fatigue-inertia and confusion-bewilderment), cholesterol, triacylglycerol, LDL cholesterol, HDL cholesterol, β -hydroxybutyrate concentrations ; serum AA:EPA, insulin, C-reactive protein, 24-hr urinary calcium concentrations
Are the methods quantitative or qualitative?	Quantitative and qualitative methods
Safety Results	<p>Creatinine Clearance Values</p> <p>These did not exceed baseline values at week 6 but at 2 weeks for the KLC they were 20% above baseline. A higher creatinine clearance rate may be a normal physiologic response but in persons with a compromised renal function complications may occur.</p>

APPENDIX A5: Data Collection Sheets – Johnston et al. (2006)

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Safety Results contd.	<p>Hence persons at risk of kidney disease should carefully consider KLC diets.</p> <p>AA: EPA was 90% higher after week 6 on the KLC. As inflammation is associated with faster rates of kidney function loss and elevated ratios of fatty acids is associated with increased inflammation and tumouregeneration in rat models.</p> <p>Plasma uric acid and urinary calcium typically higher with high-protein diets were not significantly higher at trial week 6 than at baseline.</p>
Endpoint/ Biomarker Tested	Body Weight , Fat mass, fat free mass, hunger ratings, feelings of vigour-activity, 6 distinct mood states (tension-anxiety, depression-dejection, anger-hostility, vigour-activity, fatigue-inertia and confusion-bewilderment), cholesterol, triacylglycerol, LDL cholesterol, HDL cholesterol, β -hydroxybutyrate concentrations ; serum AA:EPA, insulin, C-reactive protein, 24-hr urinary calcium concentrations
Are there end points other than those reported that might be relevant and important	Apo Lipoprotein a and b.
Are the endpoints relevant to actual practice	Yes
Dietary Intake and Adherence Results	Dietary intake as prescribed. No specific report on adherence.
Weight loss and cardio-protective mechanisms identified,	Reduced Hunger likely to result from protein intake level.
Weight Loss / Body Composition results	<p>At the end of the 6 week trial the total weight loss did not differ significantly between the diet groups (6.3 ± 0.6 and 7.2 ± 0.8 for KLC and NLC dieters respectively; $P=0.324$).</p> <p>The mean change in total weight during the self-monitored adherence phase (weeks 7-10) was also not significantly affected by diet (-1.4 kg and 0.1 for NLC and KLC respectively; $P=0.114$)</p> <p>The reduction in fat mass over the 6 week trial was also was not significantly affected by diet (5.5 and 3.4kg for NLC and KLC respectively; $P=0.114$).</p> <p>Fat- free mass did not change significantly during the 6 week trial but BMI was significantly lower after 6 weeks in both diet groups.</p> <p>Hunger ratings improved over the 6 week trial in both diet groups from “no particular feeling” to “satisfied”- $P=0.078$) and did not differ significantly between the two groups.</p> <p>Feelings of vigour activity as measured by the POMS questionnaire was greater for the NLC compared with the KLC during the trial; $P=0.025$.</p>

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Cardiac Risk Factor Results	<p>Compared with baseline, the 6 week LDL concentrations increased for 5 KLC dieters and decreased in the remaining 4 KLC dieters. In comparison LDL cholesterol was raised in 2 NLC dieters and decreased in the remaining 8 NLC dieters. HDL cholesterol concentrations fell 9% during the 6 week trial in both diet groups.</p> <p>Hepatic function as indicated by serum Y- glutamyltransferase concentration was favourably affected by the dietary treatments which were also directly related to impaired glucose tolerance.</p>
Hormonal and Endocrine results	Insulin sensitivity was significantly improved by both LC diets
Exercise and Medication use	Not Reported
What effect may bias have on the result?	Lead Authors connection with Zone Diets may have created bias in favour of the non ketogenic diet
The Author's conclusions - are these justified?	<p>Differentiating between ketogenic and non ketogenic LC diets is important for clinical practice because ketogenic diets have been associated with adverse metabolic events included elevated LDL and cardiac complications</p> <p>In this study the KLC did not offer any metabolic advantage over the NLC.</p> <p>Both diets were effective at reducing total body mass and insulin resistance.</p> <p>The KLC diet was associated with elevated blood ketones directly related to LDL cholesterol concentrations and inflammatory risk.</p> <p>Hence severe restrictions in dietary carbohydrate are not warranted.</p> <p>The NLC was associated with feelings of high energy and a favourable mood profile. Authors recommend that low-fat meats and vegetables, 8-9 daily servings of fruit and vegetables are included and a dietary carbohydrate limit near 100-125 g/d.</p> <p>Patients should be advised that there is no metabolic advantage associated with ketosis during dieting.</p>
Generalizability- the extent to which the results might apply outside the study	Results are relevant for individualisation of diet plans

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Discussion points	<p>Under isocaloric conditions total weight loss and fat loss did not differ significantly by diet treatment.</p> <p>According to weight loss averages during the self-monitored follow-up period dietary compliance may be more easily achieved with NLC than KLC.</p> <p>Reductions in total and LDL cholesterol did not differ significantly by group but 9% of variation in LDL cholesterol was directly related to blood ketone concentrations and several KLC dieters had marked increases in LDL cholesterol. Hence blood lipid concentrations should be monitored in persons who are following ketogenic diets.</p> <p>As in other weight loss trials, insulin resistance (HOMA index units) decreased in both diet groups (30%; $P < 0.05$) and body mass explained nearly 20% of the variance.</p> <p>The greater success of LC diets than the conventional low-fat HC diet with respect to weight loss has been attributed to the maintenance of previous REE during active weight loss and to reduced hunger but it is unclear whether these factors are related dietary carbohydrate restriction or to increased dietary protein. Weight adjusted REE increased in both diet groups increased over the 6 week trial but blood β-hydroxybutyrate concentrations were not correlated with REE ($r = -0.014$, $P = 0.921$) which indicates that the protein content of the diet rather than the severity of the carbohydrate restriction contributed to the increased REE.</p> <p>These data support the contention that calorie-reduced diets high in protein facilitate weight loss by partly preserving the metabolic rate. Fat-free mass – the major determinant of REE was not correlated with REE in this trial and cannot explain the observed increases in metabolism.</p> <p>Exercise and activity levels remained constant during the trial. It is possible that the high-protein diet increased body protein turnover and peptide bond synthesis and hydrolysis – processes that require ATP and utilise energy.</p> <p>Weekly ratings of perceived hunger did not differ by diet which suggests that is the protein content of the diet and not the amount of dietary restriction of carbohydrates that affects perceived hunger.</p> <p>The data suggests that in the context of high-protein diets small differences in dietary carbohydrate (as little as 50-60g /day) may affect emotion, mood state and potentially the desire to be physically active.</p>
Were study limitations discussed?	Study was limited by the small sample size. Nonetheless the data offer important insights about metabolic consequences of low-carbohydrate dieting.
Future Implications discussed	The relevance of ketogenic diets in favour of a non ketogenic diet is questioned. A more balanced approach to low-carbohydrate diets is recommended with the inclusion of low-fat meats and dairy products, 8-9 daily servings of fruit and vegetables and dietary carbohydrate near 100-125 g/d

APPENDIX A6: Data Collection Sheets- Layman et al. (2004)

(Text and/or data extracted verbatim from study article for many of the descriptive sections. Figure, Table and Numerical references included in brackets refer to the original article).

Author	Layman, Evans, Baum, Seyler, Erickson & Boileau (2004)
Title	Dietary Protein and Exercise have additive effects on Body Composition during Weight Loss in Adult Women
Journal	Journal of Nutrition of the American Society for Nutritional Sciences
Quality of Journal and competence of Researchers	Peer reviewed journal. Donald Layman- Professor Emeritus of Nutrition. Department of Food Science and Human Nutrition. Richard A. Boileau . Professor Emeritus of Kinesiology Department of Kinesiology and Community Health Applied Health Sciences.
General Aim Clear	To evaluate interactions of diet composition and exercise on body composition changes and blood lipids during weight loss
Specific Study objectives stated	To compare 2 isocaloric diets – a high-protein / low-carbohydrate (HP/LC) with a low-protein/high carbohydrate (LP/HC) diet with and with no exercise on body composition.
Aim and study objectives relevant to research question being explored External Validity - relevance of this particular piece of work to the issue under scrutiny	Relevant to primary research question as to whether the macronutrient composition of a diet is significant to weight management and CVD risk management A moderate-carbohydrate Zone type diet with and without the inclusion of exercise compared to a higher-carbohydrate conventional diet protocol with and without exercise.
Internal Validity - methods and actual results in the light of study objectives	Not controlled – Comparative intervention
Study described as randomised	Yes. Randomised 4 month weight loss trial using a 2X2 block design (Design X Exercise). The 4 groups were the protein and exercise (PRO+EX), carbohydrate and exercise (CHO+EX), a protein group (PRO) and a carbohydrate group (CHO).
Study described as double blind	No
Description of withdrawals and dropouts present	No
Randomisation / blinding appropriate	Due to resource shortage , the first 24 women were randomly assigned to either the PRO+EX or the CHO+EX groups (n=12 each)and the next 24 were randomly assigned to either the PRO or CHO groups (n = 12 each).
Target Population	Adult women
Why was study done? What was perceived general importance?	To assess the ideal balance of macronutrients necessary to optimize the combined effects of exercise and energy restriction

APPENDIX A6: Data Collection Sheets- Layman et al. (2004)

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Is there a clear hypothesis and objectives?	The hypothesis was that a diet with increased protein and reduced CHO combined with an exercise program of aerobic activity and resistance training produce an additive effect on loss of body fat and maintenance of fat free mass (FFM). The aim of the study was also to measure the effects of diet treatments and exercise on changes in blood lipids and various indicators of metabolic change during weight loss including blood concentrations of leptin, adiponectin, ghrelin and insulin.
What specific question is being addressed?	There are few studies that provide direct evidence about the combined merits and interactions of specific diet and exercise choices. Furthermore, the ideal balance of macronutrients (carbohydrates, lipids, and protein) necessary to optimize the combined effects of exercise and energy restriction is unknown.
The study setting- where did study take place?	University of Illinois
The study population - Intended group to whom results should apply vs. group actually studied	Overweight and obese Adults
Group actually studied	Women ($n = 48$) aged 40–56 y were recruited to participate in a weight loss study. Exclusion criteria were BMI < 26 kg/m ² , body weight > 140 kg (due to DXA scanning bed constraints), smoking, any existing medical conditions requiring medications that would affect primary or secondary outcomes of the study, use of oral steroids or use of anti-depression medication.
The social, cultural, economic, ethnic background	Not provided. Recruitment process not explained. Due to resource shortage , the first 24 women were randomly assigned to either the PRO+EX or the CHO+EX groups ($n=12$ each)and the next 24 were randomly assigned to either the PRO or CHO groups ($n = 12$ each).
Study Approval	Study approved by the Institutional Review Board at the University of Illinois at Urbana-Champaign
Was there clear inclusion and exclusion criteria and explanations of patient drop out?	Women aged 40-56 y were recruited Exclusion criteria were BMI <26 kg/m ² ; body weight >140kg; smoking; any existing medical conditions requiring medications that would affect primary or secondary outcomes of the study; use of oral steroids or anti-depression medication. No explanation of study dropout if any.
Is there a power calculation to determine sample size?	None Available
Was there selection bias?	Potentially possible. Recruitment process not explained.

APPENDIX A6: Data Collection Sheets- Layman et al. (2004)

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Was there funding bias?	None evident. Authors interest in promoting high-protein weight loss plans was supported by the National Cattlemen's Beef Association, The Beef Board and Kraft Foods
Confounding Factors	None evident
How does the study group relate to researchers interest groups / patients?	The researcher's interest groups would potentially include overweight women with a desire to lose weight or improve metabolic markers and understanding the impact of exercise with diet.
What was the intervention and how was it carried out?	The CHO diet provided dietary protein at 0.8g/Kg/d (15% of energy intake) with a CHO: PRO ratio >3.5 and dietary lipids at approx 30% of energy intake. The PRO diet provided dietary protein at 1.6 g/kg/d (30% of energy intake with a CHO: PRO ratio <1.5 and dietary fats at 30%. Hence the PRO Diet resembles a Zone type diet. Institute of Medicine minimum RDA for CHO =130g/d, PRO=0.8 g/kg and with upper limits for CHO <65% ad protein <35% of total energy intake resembling a conventional low-fat/high carbohydrate diet. The two diets were designed to be equal in energy 1700kcal , total fat intake 57g and fibre 17g
What was the intervention and how was it carried out? Contd.	Both diets emphasized use of high quality proteins including meat dairy eggs and included 5 servings/day of vegetables and 2-3 servings of fruit. Exercise treatments Control Group: NIH Guidelines for weight Management including 30 min of walking 5d/wk undertaken voluntarily. Exercise monitored daily via activity logs on 3d/month. Subjects wore accelerometers. Control group averaged 100min/wk of added exercise. The EX Group required walking 5d/wk for 30min/d plus a resistance training programme 2 d/wk consisting of 30 min stretching and resistance using 7 nautilus weight machines. EX subjects were required to complete a minimum of one 12 repetition set on each machine with resistance weight selected to elicit fatigue by the final repetition.
What was measured and how was it measured?	Protocol: All subjects participated in a baseline evaluation period that included a 24 h food recall, a 24 h food recall, instructions for weighing and recording of foods, two 3-d weighed foods records and measurement of bodyweight, height and blood lipids.
Were baseline measures used?	Age, height (cm), Weight (Kg), BMI (kg/m2). Baseline characteristics did not differ among subjects in each of the treatment groups. Baseline characteristics did not differ among the different treatment groups. Subjects had a mean age of 46.6 y weight of 87.7kg BMI of 32.9 and relative body fat of 44.1%. Due to wave recruitment there was a difference in BMI (P=0.047) largely associated with the difference between the CHO and CHO+EX groups.
Were process measures used?	Body weight measured using an electronic Scale – Tanita Model BWB-627A. Whole body composition and trunk fat determined by DEXA scans by the same technician using standard manufacturer guidelines. Plasma leptin, adiponectin, ghrelin and insulin were determined by commercial RIA kits with all samples for a given sample

APPENDIX A6: Data Collection Sheets- Layman et al. (2004)

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Were process measures used? contd.	<p>analysed in a batch.</p> <p>Serum total cholesterol (TC), HDL-C and TAG were determined by standardized methods by the Washington University School of Medicine Core Laboratory for Clinical Studies. LDL cholesterol was calculated using the Friedwald equation.</p> <p>Diet: Subjects were provided electronic food scales and instructed to weigh all food servings at all meals. They were required to report a 3-d weighed food record for each week throughout the study. Nutrient intakes were evaluated as mean daily intakes from 3-d weighed records using nutritionist Pro software (First DataBank). After baseline data collection, subjects received instruction from a research dietician about their specific diet and walk-in programme. During the 16 wk weight loss programme subjects were required to attend a 1 hr meeting each week at the research facility.</p> <p>Each week subjects were weighed in light clothing without shoes and turned in the 3-d weighed food records and daily activity logs.</p> <p>Statistics: All data analyses conducted using SPSS version 12.0. Differences at baseline were evaluated using one-way ANOVA with further evaluation using Fisher's least significant test. Pre-test vs. post test values within a group were evaluated by a Student's t- test.</p> <p>The primary analysis to evaluate the relative effect of the diet and exercise treatments used a 2-way ANOVA (Diet X Exercise) and the change over time as the dependent variable.</p> <p>To evaluate treatment effects on hormones, controlling for changes in body composition, an analysis of covariance (ANCOVA) was used where indicated.</p>
Were outcome measures identified? Are there clear validated outcomes?	Yes
Are the methods quantitative or qualitative?	Quantitative and Qualitative
Safety Results	None discussed.
Endpoint/ Biomarker Tested	<p>Body Weight markers: body weight, fat mass, trunk fat, lean mass</p> <p>Endocrine markers of obesity: Plasma concentrations of leptin, insulin, ghrelin and adiponectin.</p> <p>Blood lipids: TC, LDL-C, HDL-C and TAG.</p>
Are there end points other than those reported that might be relevant and important	Apo lipoprotein a and b as a significant risk factor for CVD disease along with HDL and triglycerides would have been relevant and important.

APPENDIX A6: Data Collection Sheets- Layman et al. (2004)

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Are the endpoints relevant to actual practice	Yes
Dietary Intake and Adherence Results	<p>Daily energy intakes at baseline from 3-d weighed food records were 2138 kcal/d for all subjects. Daily menus were designed to provide 1700kcal/d but subjects were free-living and ultimately determined final daily energy intake. Reductions in energy intake from weekly 3-d weighed food records did not differ among groups shown by non-significant Diet and Exercise main effects and interactions.</p> <p>Subjects in the PRO groups maintained protein intakes of 107g/d and approx 30% of energy intake. The ratio of CHO: PRO was 1.24. Total dietary lipid intake decreased to 49g/day (32% of dietary energy) and SFA decreased to 19.1 g/d (12.4% of energy)</p> <p>Subjects in the CHO groups maintained CHO intake at 198g/d (61% of energy) and reduced lipid intake to 37g/d (25.5 of energy) and SFA to 11g/d (7.5 % of energy). Protein intake was 57g/d (18% of energy intake) and the ratio of CHO:PRO was approx 3.5</p>
Weight loss and cardio-protective mechanisms identified,	<p>Protein sparing effects of increased protein on lean body mass</p> <p>Increased loss of body fat associated with lower insulin response to the reduced CHO diet</p> <p>Reduced metabolic efficiency produced by increased dietary ratio of protein to CHO</p>
Weight Loss / Body Composition results	<p>All groups lost significant body weight during the 16 week treatment period.</p> <p>Body weight changes were larger ($P<0.05$) in the groups consuming higher protein and reduced CHO.</p> <p>The PRO and PRO+EX groups had a weight loss of 9.3 ± 0.8 kg after 16 weeks while the CHO and CHO+EX groups reduced body weight by 7.3 ± 0.5 kg ($P<0.05$).</p> <p>The PRO+EX group had the largest relative weight loss at 11.2% and the CHO group had the smallest relative weight loss at 8.4%.</p> <p>Changes in body composition indicated that weight loss was predominantly fat mass and there were increased fat losses associated with the higher protein diet and the exercise program.</p> <p>Subjects in the PRO +EX and the CHO +EX groups reduced body fat by 7.2 ± 0.7kg whereas subjects not in the supervised exercise program reduced body fat by 5.5 ± 0.5kg ($P<0.05$).</p> <p>The PRO and EX effects were independent and additive.</p> <p>Specifically the combined effects of the PRO diet and the EX program produced a 21.4 % decrease in absolute body fat.</p> <p>Subjects in the CHO group without exercise had a 12.8% reduction in absolute body fat.</p> <p>Changes in absolute trunk fat were similar to changes in total fat mass with reduction in trunk fat for the PRO groups greater than the CHO groups.</p> <p>Change in trunk fat relative to change in whole body fat reduced significantly in all treatment groups with the PRO+EX group having the greatest ratio reduction of -0.028 ± 0.007 ($P=0.001$) and the CHO group experiencing the least change -0.015 ± 0.005 ($P=0.009$) however there was no significant main effect for diet ($P=0.32$) or exercise ($P=0.12$).</p> <p>Changes in lean mass reflected a significant positive effect of the exercise program ($P<0.001$) and a trend for a beneficial effect of the PRO diet ($P=0.10$).</p> <p>The PRO+EX group had no significant change in lean mass whereas the CHO had the largest decrease in lean mass.</p>

APPENDIX A6: Data Collection Sheets- Layman et al. (2004)

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Weight Loss / Body Composition results- Contd.	<p>The additive effects of the PRO+EX on body composition were apparent with significant main effect of Diet ($P<0.01$) and exercise ($P<0.001$).</p> <p>Subjects in the PRO and PRO+EX groups reduced body fatness by 4.3% whereas subjects in the CHO and CHO+EX groups reduced relative body fatness by 2.9%.</p> <p>The subjects in the PRO +EX and CHO+EX groups reduced relative body fat by 4.7% where non-exercising subjects reduced body fatness by 2.5%</p>
Ketonuria Results	None noted. CHO at 30% of energy intake.
Cardiac Risk Factor Results	<p>Initial serum lipid concentrations did not differ among all groups. After 16 wk of weight loss, changes in TC, LDL were greater in the CHO and the CHO+EX than in the PRO Groups</p> <p>Serum TC in the CHO and CHO+EX groups decreased by 0.51 ± 0.09mmol/L (9.2%) and LDL-C decreased by 0.38 ± 0.08mmol/L (10.4%) from baseline values.</p> <p>In the PRO and PRO+EX groups these decreased by 0.21 ± 0.12mmol/L (3.7%) and 0.08 ± 0.11 mmol/L (1.7%).</p> <p>Changes in TAG were highest in the PRO groups by 0.32 ± 0.06mmol/L (20.2%). In the CHO and CHO+EX groups TAG concentration decreased by 0.1 ± 0.07 mmol/L(5.2%).</p> <p>HDL-C concentrations changed in opposite directions for the 2 diet treatments. The PRO groups had a net increase of 0.01 ± 0.03mmol/L in HDL-C and the CHO groups decreased by 0.08 ± 0.03mmol/L.</p> <p>Ratios of TAG/HDL were more responsive to the PRO diet than the CHO diet</p> <p>No significant effects of EX were apparent for any lipid outcomes.</p>
Endocrine markers and Hormonal Effects	<p>Each of the 4 hormones responded to weight loss.</p> <p>Plasma concentration of leptin and insulin decreased and adiponectin and ghrelin increased.</p> <p>Only adiponectin showed treatment specific changes</p> <p>Blood concentrations of adiponectin doubled in the EX groups ($P<0.05$). After controlling for change in fat mass, the main effect of EX remained significant ($P=0.02$)</p>
Exercise and Medication use	<p>Exercise was a significant part of the treatment protocol.</p> <p>Exercise treatments</p>

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Exercise and Medication use contd.	Control Group: NIH Guidelines for Weight Management including 30 min of walking 5d/wk undertaken voluntarily. Exercise monitored daily via activity logs on 3d/month. Subjects wore accelerometers. Control group averaged 100min/wk of added exercise. The EX Group required walking 5d/wk for 30min/d plus a resistance training programme 2 d/wk consisting of 30 min stretching and resistance using 7 nautilus weight machines. EX subjects were required to complete a minimum of one 12 repetition set on each machine with resistance weight selected to elicit fatigue by the final repetition.
What effect may bias have on the result?	None evident
The Author's conclusions - are these justified?	Subjects in both diet treatments were successful in reducing daily energy intake, achieving macronutrient goals and reducing body weight and body fat mass. Subjects consuming a PRO diet with CHO:PRO ratio <1.5 lost more total weight and body fat and less lean mass compared with CHO diet group with a CHO:PRO ratio >3.5. Exercise increased loss of body fat and preserved lean mass. This study adds to body of evidence supporting protein-sparing effects from higher protein intakes during energy restriction.
Generalizability- the extent to which the results might apply outside the study	The question of dietary and macronutrient management with or without exercise and the level of exercise relevant to weight loss remains an important issue relevant to obesity studies and the general client base of the researcher.
Discussion points	<p>The study demonstrates interactions between the macronutrient content of diet and exercise during weight loss. Subjects consuming more protein and less carbohydrates lost more weight and fat mass and tended to lose less lean mass ($P=0.1$) than groups consuming more carbohydrates.</p> <p>Exercise increased the loss of body fat and preserved lean mass.</p> <p>The combined effect of diet and exercise was found to be additive for correcting body composition.</p> <p>The PRO +EX group exhibited the greatest loss of body fat -8.8kg with minimal change in lean mass -0.4kg whereas the CHO group had the least change in body fat -5.0kg and the greatest loss of lean mass -2.7kg.</p> <p>Daily energy deficits were comparable across all treatment groups.</p> <p>This study is consistent with other short term weight loss studies that show that diets with reduced CHO and increased protein result in increased weight loss and increased loss of body fat and reduced loss of lean body mass. Similarly confirms other study results that supplemental exercise tends to increase weight loss but has greater effects on body composition through preserving lean body mass whilst increasing fat loss.</p> <p>There was a main effect of diet on total weight loss with no added effect of exercise.</p>

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Discussion points- Contd.	<p>There was an absence of a main effect of exercise on weight loss consistent with other studies that weight loss by exercise requires >30 min/d and increases in lean tissue may reduce changes in total body weight. For fat loss there were main effects of both diet and exercise indicating that the effects of HP, RC (reduced Carbohydrate) and Exercise had a main effect of reducing loss of lean tissue</p> <p>Hormone changes reflect decreases in body fat mass. Plasma leptin decreased with weight loss, ghrelin increased and adiponectin showed exercise specific changes.</p> <p>Low plasma adiponectin positively associated with metabolic syndrome X – increased BMI, body fat percentage and blood TAG and reduced HDL-C. Weight reduction by energy restriction increases plasma adiponectin. Exercise of short duration does not alter body weight or body fat or adiponectin levels.</p> <p>Blood lipids are influenced more by diet than exercise. CHO groups had larger reductions in TC and HDL-C while PRO groups had greater reductions in TAG and maintained higher circulating levels of HDL-C. These results are consistent with previous studies. Blood lipids respond to both changes in body weight and dietary macronutrient content. This study raises the question about the relative merits of expressing dietary intakes of macronutrients as a percentage of energy or absolute amounts. The study design provided protein at 0.8 and 1.6g/kg/d based on specific requirements for leucine.</p> <p>At the baseline the CHO group had mean protein of 78.0g/day or 0.89g/kg/d. Energy restriction decrease in protein to 57g/d or 0.71 g/kg/d. Although this is 17% of reduced energy intake it is below minimum RDA value of 0.8g/kg/day. This may explain part of the loss of lean mass. Similar concern about percentage of energy vs. Absolute amounts for dietary lipids. Subjects in the PRO groups reduced dietary intake of lipids by 30.1g/day and SFA by 7.5g/day. Total lipids were 31.9% and SFA for 12.4% of total energy which are higher than current guidelines.</p>
Were study limitations discussed?	<p>None discussed. Lack of proper details about the recruitment process, no details of the drop-out rates or non completers, the wave and block randomisation which may have introduced bias, the short term of the study and the small sample studied are all potential limitations of the study.</p>
Future Implications discussed	<p>Differential effects of the diet and exercise treatments suggests that specific treatments may be more beneficial for specific individuals e.g. an individual with familial hypercholesterolemia may benefit from a low fat CHO diet likely to produce changes in TC and LDL while an individual with high triglycerides and low HDL, T2D may benefit from the PRO diet. Further research required for individualisation of dietary macronutrients based on phenotypes can improve long term treatment of obesity and associated health risks.</p>

APPENDIX A7: Data Collection Sheets – Luscombe-Marsh et al. 2005

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Author	Luscombe-Marsh et al. (2005)
Title	Carbohydrate-restricted diets high in either monounsaturated fat or protein are equally effective at promoting fat loss and improving blood lipids.
Journal	The American Journal of Clinical Nutrition.
Quality of Journal and competence of Researchers	Peer reviewed Journal. Luscombe- Marsh PhD from Adelaide University, post-doctoral position at the University of Maastricht, The Netherlands. Manny Noakes and Peter M Clifton both PhDs
General Aim Clear	This study explores a pertinent question arising from previous studies that whether, in the context of carbohydrate-restricted diets, the high-protein or the high-fat modification is potentially better at promoting fat loss and improving cardiovascular and diabetes risk.
Specific Study objectives stated	<p>The objective of the present study was to compare the short-term effects of 2 isocaloric, energy restricted, carbohydrate-matched diets that were either low-fat, high-protein (LF-HP) or high-fat, standard-protein (HF-SP; monounsaturated-fat enriched) on weight loss, body composition, energy expenditure, appetite, glucose, insulin, and lipid metabolism in subjects with insulin concentrations >12 mU/L.</p> <p>The short-term effects of the 2 moderate-carbohydrate dietary prescriptions on markers of bone turnover, inflammation, and renal function were also examined.</p>
Aim and study objectives relevant to research question being explored External Validity - relevance of this particular piece of work to the issue under scrutiny	<p>Relevant to primary research question as to whether the macronutrient composition of a diet and particularly carbohydrate (CHO) restriction is significant to weight management and CVD risk management. Particularly relevant in assessing effects of the level of CHO that may be recommended.</p> <p>2 carbohydrate restricted diets included in design with carbohydrates restricted to 30% of energy with differing levels of protein and fat. These were classified as low-carbohydrate non-ketogenic diets.</p>
Internal Validity - methods and actual results in the light of study objectives	Parallel randomized study.
Study described as randomised	The 73 subjects accepted for participation in the study were sorted into pairs matched for fasting serum insulin, BMI, age, and sex. The resulting matched groups were randomly assigned to either the low-fat, high-protein (LF-HP) 30% Fat and 40% Protein diet or the high-fat, standard-protein (HF-SP) diet with 50% Fat and 20% protein.
Study described as double blind	No

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Description of withdrawals and dropouts present	Yes. Seventy-three obese men and women were recruited through public advertisement. 36 (13 men and 23 women) assigned to the LF-HP group and 37 (13 men and 24 women) assigned to the HF-SP group. 5 dropouts prior to start of intervention – 1 LF and 2 LF could not be contacted; 1 HF due to work commitments; 1LF for family reasons leaving 34 in each group (13 men and 21 women). 11 dropouts before end of intervention – 7 in LF group and 4 in HF group. Reasons given. Leaving 30 in the HF-SP group and 27 in the LF-HP group.
Randomisation / blinding appropriate	73 subjects accepted were sorted into pairs matched for fasting serum insulin, BMI, age and sex. The resulting matched groups were randomly assigned to either the low-fat, high-protein (LF-HP) or high-fat, standard protein (HF-SP).
Target Population	Obese Adults who were generally in good health.
Why was study done? What was perceived general importance?	In the context of carbohydrate restricted diets is the high-protein or the high-fat modification potentially better at improving cardiovascular and diabetes risk.
Is there a clear hypothesis and objectives?	To compare the short-term effects of 2 isocaloric (1500kcal per day) energy-restricted , moderate but matched (30%) carbohydrate diets, that were either low-fat, high-protein (LF-HP) or high-fat, standard protein (HF-SP).
What specific question is being addressed?	Together with moderate carbohydrate, is lowering fat or lowering protein more effective for improving CVD and diabetes risk
The study setting- where did study take place?	University of Adelaide
The study population - Intended group to whom results should apply vs. group actually studied	73 Obese men and women (26 men and 47 women) with BMI between 27 and 40; Aged between 20 and 65y.
The social, cultural, economic, ethnic background	Not much known about the social cultural or ethnic background of the subjects.
Study Approval	All experimental procedures followed the ethical standards of and were approved by the Human Ethics Committees of the Commonwealth Scientific Industrial Research Organisation (CSIRO) and the Royal Adelaide Hospital. All participants gave written informed consent.
Was there clear inclusion and exclusion criteria and explanations of patient drop out?	A screening session was conducted, and subjects were included if they were aged between 20 and 65 y, were nondiabetic, had a fasting serum insulin concentration >12 mU/L, and a body mass index (in kg/m ²) between 27 and 40.
Is there a power calculation to determine sample size?	The study had 80% power ($\alpha = 0.05$) to detect differences between dietary groups of 3.6 kg in body weight, 0.9 kg in lean and fat mass, 3 mU/L in fasting insulin, 0.2 mmol/L in LDL cholesterol, and 7% in REE.

APPENDIX A7: Data Collection Sheets – Luscombe-Marsh et al. 2005

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Was there selection bias?	None evident
Was there funding bias?	Supported in part by the National Health and Medical Research Council of Australia. No bias evident.
Confounding Factors	None noted
How does the study group relate to researchers interest groups / patients?	Obese and overweight are within the clinical interest area of the researcher.
What was the intervention and how was it carried out?	<p>The protocol and potential risks and benefits of the study were fully explained to each subject before he or she provided written informed consent.</p> <p>The 16-wk intervention was divided into a 12-wk period of energy restriction followed by 4 wk of energy balance.</p> <p>At weeks 0, 2, 4, 6, 8, 10, 12, 14, and 16, measurements of body weight were made and diet counselling was given.</p> <p>At weeks 0, 4, 8, 12, and 16, measurements of blood pressure were made and venous blood was collected.</p> <p>In addition, at weeks 0 and 16, 24-h urine samples were collected.</p> <p>Subjects taking antihypertensive or lipid lowering medication were asked to maintain all medications and supplements at pre-study doses.</p> <p>Most subjects were sedentary at baseline and were asked to continue their usual physical activity levels and to refrain from drinking >2 standard glasses of alcohol per week throughout the study.</p> <p>The prescribed diets were:</p> <p>1) a LF-HP diet containing 30% of energy as fat (46 g/d) and 40% of energy as protein (136 g/d), and</p> <p>2) a HF-SP diet containing 50% of energy as fat (76 g/d) and 20% of energy as protein (67 g/d).</p> <p>For each diet, the percentages of energy derived from carbohydrate and saturated fat were matched; carbohydrate was restricted to 30% of energy (approximately 110 g/d), and saturated fat was restricted to <10% of energy. The fibre content of each diet was similar (21 g/d in the LF-HP diet and 27 g/d in the HF-SP diet).</p> <p>To achieve the composition of the prescribed diets, the subjects followed fixed-menu plans and were supplied with key foods that made up 60% of their energy intake.</p>

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<p>What was the intervention and how was it carried out? – Contd.</p>	<p>Foods were provided at 2 weekly intervals when the subjects visited the research unit for dietary counselling.</p> <p>The subjects were counselled by a dietician on the dietary protocol and on how to keep daily dietary intake checklists for all foods eaten.</p> <p>The subjects' body weights and dietary intake checklists were monitored every 2 wk, and dietary adjustments were made if the food specified was too little or too much.</p> <p>Three consecutive days (1 weekend day and 2 weekdays) of the checklists from each 2-wk period were analyzed with the use of DIET/1 NUTRIENT CALCULATION software (1998; Xyris Software, Highgate Hill, Australia), a computerized database of Australian foods.</p> <p>The study was conducted on an outpatient basis over 16 wk.</p> <p>Both dietary groups underwent 12 wk of energy restriction (approximately 6000 kJ/d, or 1433 kcal/day or 30% restriction of total energy) followed by 4wk in energy balance with the same macronutrient composition. If an individual was not achieving the desired weight loss of 0.5–1 kg/wk during the energy-restricted phase, or if during the energy balance phase he or she did not maintain a stable weight, minor adjustments in food intake were made at the fortnightly diet counselling sessions.</p> <p>The test meals were LF-HP (2636 kJ, 37% of energy as protein, 30% fat, 32% carbohydrate) and HF-SP (2586 kJ, 18% of energy as protein, 49% fat, 32% carbohydrate)</p>
<p>What was measured and how was it measured?</p>	<p>On 2 consecutive days at weeks 0, 4, 8, 12, and 16, body weight, blood pressure, and venous blood samples were taken in the morning after the subjects had fasted overnight for measurement of blood glucose, insulin, and lipid concentrations.</p> <p>At weeks 0 and 16, a single venous blood sample was taken for the determination of serum creatinine, and a 24-h urine sample was collected for the assessment of the ratio of urea to creatinine to determine dietary compliance.</p> <p>Calcium and sodium excretion, as well as ratios of deoxypyridinoline to creatinine and of pyridinoline to creatinine (biomarkers of bone turnover) were assessed from the 24-h urine sample at weeks 0 and 16.</p> <p>Also at weeks 0 and 16, measurements of body composition and total energy expenditure and a 3-h meal tolerance test using meals that were representative of the diet to which the subjects were assigned were performed.</p> <p>Venous blood samples for the determination of glucose, insulin, and free fatty acid concentrations were taken before the subjects</p>

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<p>What was measured and how was it measured? – contd.</p>	<p>had their test meals as well as 30, 60, 120, and 180 min after the meal.</p> <p>Resting energy expenditure (REE), the thermic effect of feeding (TEF), respiratory quotient (RQ), and appetite sensations (hunger, satiety, fullness, and desire to eat) were also measured before and after the meal at these time points.</p> <p>Body weight (model AMZ14 digital scale; A&D Mercury, Kinomoto, Japan) was recorded while the subjects were wearing light clothing without shoes. Total fat mass and total lean mass were assessed by whole-body dual-energy X-ray absorptiometry (densitometer XR36; Norland Medical Systems)</p> <p>Thirty subjects (6 men and 8 women from the LF-HP group and 6 men and 10 women from the HF-SP group) were recruited to participate in the energy expenditure measurements performed at weeks 0 and 16.</p> <p>The subjects were asked to refrain from participating in planned exercise, drinking alcohol, and smoking for ≥ 12 h before the measurement of resting energy expenditure.</p> <p><i>Appetite responses</i> Hunger, fullness, satiety, desire to eat, and the amount of food desired to eat were assessed by using a 100-mm visual analogue scale before and 30, 60, 120, and 180 min after the test meal.</p> <p>The subjects were asked to make a single vertical mark on each scale somewhere between the 0- and 100-mm extremes (e.g., hungry to not hungry) to indicate their feelings at that time point. The subjects did not discuss their ratings with each other and could not refer to their previous ratings when marking the scale.</p>
<p>Were baseline measures used?</p>	<p>No significant differences existed in subject characteristics between treatment groups at baseline.</p> <p>For body weight, there was a main effect of sex such that the men were heavier than the women ($P < 0.001$). There was also a diet-by sex interaction ($P = 0.04$) such that the men in the HF-SP group weighed more than did the men in the LF-HP group ($P = 0.03$).</p> <p>Fasting plasma glucose was higher in the men than in the women (main effect of sex, $P = 0.018$).</p>
<p>Were process measures used?</p>	<p>Biochemical analyses Fasting blood samples were collected in tubes containing either serum clotting activator for the measurement of insulin, lipids, fatty acids, and creatinine or sodium fluoride-EDTA for the measurement of glucose.</p>

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<p>Were process measures used? – contd.</p>	<p>Total cholesterol, HDL cholesterol, triacylglycerols, fatty acids, glucose, and creatinine were measured on a Hitachi centrifugal analyzer (Roche, Indianapolis, IN) with the use of standard enzymatic kits.</p> <p>Assays were performed for insulin, HDL cholesterol, and LDL cholesterol.</p> <p>All biochemical assays were performed in a single run at the end of the 16-wk study.</p> <p>Homeostatic model assessment (HOMA) was used as a surrogate measure of insulin sensitivity and was calculated as fasting serum insulin (mU/L) X fasting plasma glucose (mmol/L)/22.5.</p> <p>Twenty-four– hour urine samples were collected, the volume was recorded, and aliquots were frozen until analyzed (in one run at the end of the study) for the measurement of urea and creatinine concentrations with the urease enzymatic assay.</p> <p>Urinary pyridinium and deoxypyridinium cross-links (markers of bone turnover) were measured by using HPLC.</p> <p>Creatinine clearance was computed from plasma and 24-h urine creatinine excretion as follows: creatinine clearance = [(urine creatinine concentration in mmol/L) X (urine volume in mL/1140 min)/ (plasma creatinine concentration in (μmol/L) · 1000 mL⁻¹ · min⁻¹)] X 0.7.</p> <p>Two subjects were excluded from the lipid analysis because they ceased taking lipid-lowering medications 3 subjects were unable to have a dual-energy X-ray absorptiometry scan completed at week 16.</p> <p>Statistical analysis was performed by using SPSS for WINDOWS 10.0 software (SPSS Inc, Chicago, IL).</p> <p>Baseline measurements were assessed by using two-factor analysis of variance (ANOVA) with diet and sex as the fixed factors. The effect of the diet intervention was assessed by using repeated-measures ANOVA; for each dependent variable, the measurements at weeks 0, 4, 8, 12, and 16 are the within-subject factor (i.e., time) and diet and sex are the between-subject factors.</p> <p>In specific analyses, baseline weight, cholesterol, total fat mass and total lean mass were included as covariates.</p> <p>Week 0 and 16 response curves after the test meals were compared by using repeated-measures ANOVA with week and blood sampling time as the within-subject factors and diet and sex as the between subject factors.</p> <p>When significant interactions of time-by-diet or time-by-diet-by-sex were found, paired <i>t</i> tests were used to find where the differences lay.</p>
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Were outcome measures identified? Are there clear validated outcomes?	Body weight and body composition, Resting energy expenditure, the thermic effect of feeding and respiratory quotient, Appetite responses, Biochemical analyses for measuring insulin, lipids, glucose
Are the methods quantitative or qualitative?	Quantitative and qualitative methods
Safety Results	Both diets were well tolerated, with no adverse events or effects reported.
Endpoint/ Biomarker Tested	Body weight and body composition, Resting energy expenditure, the thermic effect of feeding and respiratory quotient, Appetite responses, Biochemical analyses for measuring insulin, lipids, glucose, bone turnover, inflammation and renal function
Are there end points other than those reported that might be relevant and important	Apo Lipoprotein a and b
Are the endpoints relevant to actual practice	Yes
Dietary Intake and Adherence Results	<p>The energy and macronutrient contents derived from the subjects' daily weighed-food checklists did not differ from those of the prescribed diets.</p> <p>The percentage of energy derived from the macronutrients of both diets was not significantly different during the energy-balance compared with the energy-restricted phase.</p>
Dietary Intake and Adherence Results – Contd.	<p>Appetite The subjects did desire less to eat after the LF-HP meal than after the HF-SP meal at both week 0 and week 16 (main effect of diet, $P=0.02$). There was a significant reduction in the 3-h hunger response from week 0 to week 16 (main effect of time, $P=0.018$). In addition, there was a trend for desire to eat ($P=0.06$) and the amount desired to eat ($P=0.07$) to be reduced after 16 wk.</p>
Weight loss and cardio-protective mechanisms identified	<p>Increased protein at the expense of carbohydrates has a positive effect on insulin resistance and lipid metabolism.</p> <p>Data from an <i>ad libitum</i> feeding study (Skov 1999) suggest that the satiating effects of protein-rich foods, such as lean meat and low-fat dairy products, are responsible for the reduced energy intake (by approximately 20%) that leads to greater weight loss (by 3.3 kg) after 6 mo of a LF-HP diet (30% fat, 25% protein) than after a LF-SP diet (30% fat, 12% protein). In the present study, the amount of food desired to eat over the 3-h period after the test meal was less after the LF-HP meal than after the isocaloric HF-SP meal, which is consistent with a greater satiating effect of protein.</p>

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<p>Weight Loss / Body Composition results</p>	<p>After 12 wk of energy restriction and 4 wk of energy balance, weight loss did not differ between subjects in the LF-HP and HF-SP groups. The amounts of fat and lean mass that were lost also did not differ.</p> <p>The reduction in body weight after 16 wk was $9.5 \pm 0.9\%$, or 9.2 ± 0.7 kg (main effect of time, $P < 0.001$; 10.2 ± 1.4 kg for the HF-SP diet, 9.7 ± 1.1 kg for the LF-HP diet).</p> <p>All the weight loss occurred during the energy-restricted phase of the diet (from week 0 to week 12); no further weight loss occurred during the energy balance phase.</p> <p>The men lost 2% more of their body weight than did the women (time-by-sex interaction, $P = 0.03$).</p> <p>From week 0 to week 16, the reduction in fat mass was $13.9 \pm 1.5\%$ and the decrease in abdominal fat mass was $17.1 \pm 2.0\%$ (main effects of time, $P < 0.001$).</p> <p>Lean mass was reduced by $6.0 \pm 0.6\%$ (main effect of time, $P < 0.001$).</p>
<p>Cardiac Risk Factor Results</p>	<p>Improvements in fasting serum lipid concentrations did not differ significantly between the LF-HP and HF-SP groups, and there were no time-by-diet or time-by-diet- by-sex interactions for any of these variables.</p> <p>Total cholesterol was reduced by $6.6 \pm 1.4\%$ at week 12 compared with week 0, and it remained reduced by $2.9 \pm 1.4\%$ at week 16 (main effect of time, $P < 0.001$).</p> <p>LDL cholesterol was reduced by $3.4 \pm 1.9\%$ at week 12 and by $0.7 \pm 2.3\%$ at week 16 ($P = 0.005$).</p> <p>HDL cholesterol was increased by $6.8 \pm 2.0\%$ at week 12, and at the end of week 16 it remained $10.1 \pm 2.1\%$ above baseline ($P < 0.001$).</p> <p>The serum triacylglycerol concentration was reduced by $23.1 \pm 3.6\%$ by week 12 and by $15.9 \pm 4.3\%$ at week 16 (main effect of time, $P < 0.001$).</p> <p>The reduction in REE (regardless of whether it was expressed as an absolute value or was adjusted for body composition) did not differ significantly between the LF-HP and the HF-SP group, and there were no time-by-diet or time-by-diet-by-sex interactions for REE.</p> <p>There was no effect of diet composition on urinary calcium or sodium excretion, concentrations of bone-turnover markers, C - reactive protein (CRP) or blood pressure.</p>

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<p>Cardiac Risk Factor Results – Contd.</p>	<p>Urinary calcium and sodium excretion remained unchanged from week 0 to week 16 (3.5 ± 0.4 and 4.1 ± 0.4 mmol/24 h for week 0 and week 16 calcium values, respectively, and 181 ± 31 and 158 ± 11 mmol/24 h for week 0 and week 16 sodium values), as did concentrations of the bone-turnover markers (94 ± 5.1 and 102 ± 5.2 nmol/mmol for week 0 and week 16 pyridinoline: creatinine values, respectively, and 26 ± 1.3 and 28 ± 1.4 nmol/ mmol for deoxypyridinoline: creatinine values).</p> <p>CRP fell by $24.0 \pm 20.2\%$ (from 3.9 ± 0.4 mg/L at week 0 to 3.1 ± 0.4 mg/L by week 12; main effect of time, $P=0.001$), but by week 16 the reduction from baseline ($6.7 \pm 15.0\%$) was not significant (week 16 CRP: 3.4 ± 0.37 mg/L).</p> <p>Systolic blood pressure decreased from 130 ± 1.89 mm Hg at week 0 to 123 ± 1.5 mm Hg at week 16 (main effect of time, $P<0.001$), but diastolic blood pressure remained unchanged (72 ± 1.3 mm Hg at week 0 and 71 ± 1.0 mm Hg at week 16).</p> <p>For serum creatinine, there was no main effect of time or diet. For men, the concentration decreased from 91.5 ± 2.9 to 85.6 ± 3.3 μmol/L in the SP group ($P=0.005$) but remained unchanged in the HP group (85.3 ± 2.3 and 85.7 ± 3.0 μmol/L).</p> <p>Creatinine clearance did not change with time in either diet group (117 ± 13 and 124 ± 15 mL/min at weeks 0 and 16, respectively, in the HF-SP group, and 121 ± 10 and 141 ± 12 mL/min at weeks 0 and 16, respectively, in the LF-HP group).</p>
<p>Hormonal and Endocrine results</p>	<p>Fasting concentrations of plasma glucose remained unchanged throughout the 16 wk in both the LF-HP and HF-SP Groups.</p> <p>Improvements in fasting serum insulin, the HOMA index of insulin resistance, and in fasting serum free fatty acids were also not significantly different in the LF-HP and HF-SP groups.</p> <p>After 16 wk, the decrease in fasting serum insulin was $25 \pm 4.2\%$ (main effect of time, $P < 0.001$) and the HOMA insulin resistance index was reduced by $34 \pm 8.8\%$ ($P<0.001$).</p> <p>There was a main effect of time on fasting serum FFA concentrations ($P<0.001$); the effect was due to a $26.7 \pm 7.3\%$ increase from week 0 to week 12 ($P= 0.009$), but by week 16 the concentration had fallen and was not significantly different from that at week 0 ($P = 0.34$).</p> <p>At week 16, the increase in plasma glucose in response to the test meals was less than that at week 0. There was no significant effect of diet or any time-by-diet or time-by-diet-by sex interactions on plasma glucose responses.</p> <p>The glucose and insulin responses did not differ significantly after the LF-HP and HF-SP meals at both weeks 0 and 16.</p>
<p>Exercise and Medication use</p>	<p>The subjects were asked to refrain from participating in planned exercise.</p>

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What effect may bias have on the result?	None noted
The Author's conclusions - are these justified?	<p>In summary, in obese subjects with moderately elevated insulin concentrations, after 12 wk of energy restriction and 4 wk of energy balance, the magnitude of weight loss and the improvements in insulin resistance and lipid metabolism that were achieved with carbohydrate-restricted diets that contained either moderately increased amounts of protein or monounsaturated fat were not significantly different.</p> <p>The higher-protein meals however had the advantage of blunting the decrease in the (thermic effect of feeding) TEF observed after weight loss, and they also reduced the amount of food desired at the next meal.</p> <p>The implication of these findings is that protein from meat, poultry, and dairy foods or fat from food sources rich in monounsaturated fatty acids are both suitable options to replace some dietary carbohydrate, at least in the short term, and the choice of weight-loss diet can be tailored to individual preferences.</p>
Generalizability- the extent to which the results might apply outside the study	Results would be relevant for individualisation of diet plans
Discussion points	<p>Recent short-term studies (lasting 4–6 mo), including this study have shown positive effects of diets in which protein is increased at the expense of carbohydrate on weight loss and markers of cardiovascular disease risk, such as insulin resistance and lipid metabolism.</p> <p>None of these studies, however, were designed to determine whether the beneficial effects, particularly on markers of cardiovascular disease risk, resulted from the reduced carbohydrate or the increased protein content of the diets.</p> <p>The present study therefore matched the carbohydrate content of 2 isocaloric, energy-restricted diets and manipulated the protein-to-fat ratio.</p> <p>The main finding of the present study was that the LF-HP diet (which was based on lean meat, poultry, and low-fat dairy foods) and the HF-SP diet (which was based on lean meat, poultry, higher-fat milk, and oil and nuts high in monounsaturated fat) were both well accepted, as evident from the similar dropout rates in the 2 diet groups and compliance with the dietary prescriptions.</p> <p>The experimental diets had no deleterious effects on renal function, blood pressure, or markers of bone turnover and were equally effective at reducing body weight, improving insulin resistance, and improving cardiovascular disease risk factors.</p> <p>This finding contrasts with the results of 2 of the researchers previous studies of subjects with moderately elevated insulin</p>

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Discussion points – Contd.	<p>concentrations and type 2 diabetes, which showed statistically greater improvements in postprandial glucose responses, fasting lipid concentrations, and fat loss and lean mass preservation in women after 16 wk of a low-fat, moderate-carbohydrate, high-protein diet than after an isocaloric low-fat, high-carbohydrate, standard-protein diet</p> <p>The findings also differs from those of Layman et al (2003) and Piatti et al (1994), who both showed that the fat-to-lean mass loss ratio (an indicator of fat utilization and preservation of lean mass) is greater for women after a high protein, moderate-carbohydrate diet.</p> <p>Thus, it appears that restriction of carbohydrate in a low-fat, moderate-carbohydrate, high-protein diet may be beneficial in improving body composition compared with a low-fat, high-carbohydrate, standard-protein diet, perhaps by reducing insulin and enhancing lipolysis of stored fat.</p> <p>However, an analysis of 94 weight-loss interventions found that total weight loss or changes in fasting plasma glucose and serum lipid concentrations were not independently associated with the reduced carbohydrate intake (Bravata et al. 2003), although body composition was examined in few of these interventions. Most studies have shown that energy intake and not macronutrient composition is the key determinant of total weight loss. There is concern that replacing carbohydrate with fat may adversely affect insulin resistance and plasma lipids, although unsaturated fat probably does not have this adverse effect.</p> <p>In the present study, the increased fat content of the HF-SP diet did not have any detrimental effect on insulin resistance or the lipid profile of the subjects, who showed weight-loss-related improvements. This finding is consistent with those of others who showed improvements in the lipid profile of subjects who were hypercholesterolemic (52) or had type 1 diabetes (53) after they were placed on high-monounsaturated-fat diets.</p> <p>In the present study, CRP was reduced significantly during active weight loss by 24%; during the weight maintenance phase, however, CRP rose and the final reduction of 14% was not statistically significant.</p> <p>An effect of energy intake on CRP has not been noted before, although weight loss has been shown to reduce CRP.</p> <p>In both of these low-carbohydrate diets, fasting free fatty acids were modestly elevated during the active weight-loss phase, consistent with greater use of fat as an energy source and enhanced mobilization of fat during energy restriction.</p> <p>This study and various others have consistently shown that a high-protein compared with a standard-protein meal increases the thermic effect of food (TEF) and may also reduce the decrease in the TEF after weight loss. Similarly, in the present study, we observed that the decrease in the TEF after weight loss was approximately 3.3% smaller in the LF-HP diet group than in the HF-SP group. Even though over the short-term, the TEF does not appear to enhance weight loss, it may have some effect, albeit minimal, on weight maintenance.</p>
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Discussion points – Contd.	<p>In this study, REE was reduced after weight loss but the reduction was not affected by the protein-to-fat ratio of the diet, a finding that is consistent with our previous results.</p> <p>In the present study, the amount of food desired to eat over the 3-h period after the test meal was less after the LF-HP meal than after the isocaloric HF-SP meal, which is consistent with a greater satiating effect of protein.</p> <p>Data from an <i>ad libitum</i> feeding study (Skov 1999) suggest that the satiating effects of protein-rich foods, such as lean meat and low-fat dairy products, are responsible for the reduced energy intake (by approximately 20%) that leads to greater weight loss (by 3.3 kg) after 6 mo of a LF-HP diet (30% fat, 25% protein) than after a LF-SP diet (30% fat, 12% protein).</p>
Were study limitations discussed?	Not discussed.
Future Implications discussed	<p>Whether these mechanisms lead to differential weight loss under <i>ad libitum</i> conditions needs to be explored over the long term. The implication of these findings is that protein from meat, poultry, and dairy foods or fat from food sources rich in monounsaturated fatty acids are both suitable options to replace some dietary carbohydrate, at least in the short term, and the choice of weight-loss diet can be tailored to individual preferences.</p>

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Author	McAuley et al. (2004)
Title	Comparison of high-fat and high-protein diets with a high-carbohydrate diet in insulin-resistant obese women
Journal	Diabetologia
Quality of Journal and competence of Researchers	Peer Reviewed Journal.
General Aim Clear	To compare low-carbohydrate diets with a conventional diet in overweight women.
Specific Study objectives stated	To assess how popular low-carbohydrate diets namely the Atkins and Zone diet approaches compare with a high-carbohydrate conventional diet in Adult Women at risk of T2D due to being overweight and insulin resistant.
Aim and study objectives relevant to research question being explored External Validity - relevance of this particular piece of work to the issue under scrutiny	Relevant to primary research question as to whether the macronutrient composition of a diet is significant to weight management and cardiovascular disease (CVD) risk management. Two lower-carbohydrate diets included in the study. An Atkins type diet, Zone type diet and a low-fat/high-carbohydrate made up the three arms of the study.
Internal Validity - methods and actual results in the light of study objectives	Randomized, comparative intervention
Study described as randomised	Ninety-six normoglycaemic, insulin-resistant women (BMI >27 kg/m ²) were randomised to one of three dietary interventions: a high-carbohydrate, high-fibre (HC) diet, the high-fat (HF) Atkins Diet or the high-protein (HP) Zone Diet.
Study described as double blind	No
Description of withdrawals and dropouts present	Of the 96 eligible participants, 12 withdrew from the study. Three withdrew after baseline measurements had been made, before the start of the dietary intervention, and were not included in the analysis.
Randomisation / blinding appropriate	A random allocation sequence was generated in blocks of nine. Sequentially numbered envelopes were used to assign participants to each group. There was no stratification. It was not possible to blind researchers or participants; however, the groups were designated by codes rather than actual names to minimize cross-contamination between the groups.
Target Population	Generally healthy overweight women

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Why was study done? What was perceived general importance?	The experimental approach was designed to mimic what might be achieved in clinical practice: the recommendations involved advice concerning food choices and were not prescriptive in terms of total energy.
Is there a clear hypothesis and objectives?	To question if the conventional diet recommendation low in saturated fatty acids, rich in wholegrains, vegetables and fruit is appropriate in order to reduce the risk of obesity, CVD and do the Atkins (high-fat) and Zone (high –protein) provide suitable alternatives
What specific question is being addressed?	Is a carbohydrate-restricted weight loss programme more effective than a low-fat diet with respect to weight loss and cardiovascular risk factors?
The study setting- where did study take place?	Edgar National Centre for Diabetes Research, Medical and Surgical Sciences, University of Otago, Dunedin , New Zealand
Group actually studied	Ninety-six participants of European descent were eligible for randomisation to one of three groups by virtue of normal glucose tolerance, total cholesterol <7 mmol/l, creatinine <130 μ mol/l, normal liver function tests and reduced predicted insulin sensitivity (insulin sensitivity score ≤ 6.3 G mIU ⁻¹ l ⁻¹)
The social, cultural, economic, ethnic background	Participants of European descent.
Study Approval	The study was approved by the Otago Ethics Committee. Written consent was obtained from participants.
Was there clear inclusion and exclusion criteria and explanations of patient drop out?	Overweight women aged 30–70 years who were not pregnant or planning pregnancy, did not have a major medical condition, and were not currently undertaking a formal weight loss programme or following a strict vegetarian diet. Five hundred women responded to local advertisements regarding this study. A 75-g Overnight Glucose Tolerance Test (OGTT) was performed for 251 of the 314 potentially eligible individuals who were found to have a BMI >27 kg/m ² during a screening visit.
Is there a power calculation to determine sample size?	An earlier study indicated that the root mean square error (an estimate of SD) for weight loss, adjusted for baseline values, was 4.5 kg. This is equivalent to an effect size of 0.66 or 0.70. Two samples of 32 subjects have the potential to detect this difference with 80% power using the 5% level of significance.
Was there selection bias?	None evident.
Was there funding bias?	Study funded by the Health Research Council of New Zealand.
Confounding Factors	None identified

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How does the study group relate to researchers interest groups / patients?	The researcher's interest groups would potentially include overweight and/or obese adults. The <i>ad libitum</i> dietary approach is of particular interest.
What was the intervention and how was it carried out?	<p>There were supervised weight loss and weight maintenance phases (8 weeks each), but there was no contact between the research team and the participants during the final 8 weeks of the study.</p> <p>Although <i>ad libitum</i> consumption was advised regardless of group allocation, the first 8 weeks of the study were intended to be a weight loss phase, with dietary advice reinforced during weekly reviews.</p> <p>Similar supervision continued during the weight maintenance phase (weeks 8 to 16). From week 16 to week 24, participants were asked to continue to follow their dietary programme, but there was no contact with the research team.</p> <p>None of the diets were formally energy restricted during any phase.</p> <p>Demographic details and medical history were recorded, and a blood sample drawn for fasting glucose, insulin, lipid profile, serum creatinine and liver function tests.</p> <p>High-fat diet (Atkins Diet) -This dietary programme was based on the guidelines described in by Atkins. There were no specific macronutrient targets except for carbohydrates. During the first 2 weeks of the 8-week weight loss phase of the intervention, participants were instructed to limit certain foods in order to consume less than 20 g of carbohydrate daily.</p> <p>Participants were provided with tables indicating acceptable foods, separating restricted and free foods, and foods which had to be excluded.</p> <p>During weeks 3 to 8 of the weight loss phase, carbohydrate was reintroduced by the addition of 5 g/day each week, so that a maximum of 50 g of carbohydrate per day was consumed by week 8.</p> <p>During weeks 8 to 16 (the supervised weight maintenance phase of the intervention) the principle of increasing carbohydrate intake from the specific food lists by 5 g/day each week was continued until each participant found the maximum level of carbohydrate consumption without weight gain.</p> <p>During the unsupervised follow-up phase of the intervention, participants were encouraged to consume the amount of carbohydrate that would help to avoid weight gain.</p> <p>High-protein diet (Zone Diet): The Zone Diet recommends that of the total energy provided by each meal and snack, 40% should be from low glycaemic index carbohydrate, 30% from protein and 30% from fat (predominantly monounsaturated).</p> <p>Participants were advised to eat five times daily, with no more than 5 h between meals. The programme was presented to participants as a series of tables listing food types and serving sizes. Participants were advised to consume an appreciable amount of food from the protein table, to fill up with foods from the fruit and vegetable table, and to consume small amounts of items from</p>

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<p>What was the intervention and how was it carried out?- contd.</p>	<p>the fats and oils table. A further table listed food items to be restricted to one serving per day.</p> <p>During the supervised weight maintenance phase, subjects were instructed to consume slightly larger portions of foods in the evening to maintain their body weight. During the unsupervised follow-up phase, participants were encouraged to continue consuming appropriate foods in quantities that facilitated weight maintenance.</p> <p>High-carbohydrate, high-fibre diet (control group): The nutrient composition of this diet was based on that recommended by Diabetes and Nutrition Study Group (DNSG) of the European Association for the Study of Diabetes (EASD).</p> <p>These guidelines focus on the consumption of specific food groups in specified daily amounts and consist of the following: (1) at least six servings of breads and cereals (preferably wholegrains); (2) at least three servings of vegetables and two of fruit, with emphasis on those rich in soluble fibre; (3) at least two servings of low fat milk or milk products; and (4) at least one serving of lean meat, chicken, seafood, eggs, cooked dried beans, peas or lentils (with legumes rich in soluble fibre especially encouraged). Advice to reduce dietary fat, salt and sugar intakes was also given.</p> <p>Each guideline was followed by a table containing serving sizes, healthy choices for that food group, and foods to be restricted as much as possible. During the supervised weight maintenance phase of the intervention, participants were instructed to consume slightly larger portions for their evening meal to maintain body weight. Similar advice was given for the unsupervised follow-up phase.</p>
<p>What was measured and how was it measured?</p>	<p>All three groups had diets of similar macronutrient composition at baseline.</p> <p>All measurements were made at baseline and during the final week of each of the three experimental periods.</p> <p>Height, weight and waist circumference (at the midpoint between the anterior superior iliac crest and the lowest rib) were measured, and BMI was calculated. Blood pressure was recorded after 5 min of rest using random-zero sphygmomanometers, and a 75-g OGTT was performed, with fasting and 2-h measurements of glucose and insulin assessed.</p>
<p>Were baseline measures used?</p>	<p>Fasting samples were also obtained for lipid measurements and for assessment of high-sensitivity C-reactive protein (CRP) using a kit from Roche Diagnostics (Indianapolis, IN, USA).</p> <p>A measure of body fat was obtained using an IMP5 Bioimpedance Analyser (Impedimed, Eight Mile Plains, QLD, Australia), with subjects in a fasted state after emptying their bladders and having refrained from alcohol and exercise for the previous 24 h.</p>

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Were process measures used?	<p>Participants were given scales to weigh food and asked to complete a 3-day dietary record.</p> <p>A difference in weight loss of 3 kg between the HC diet and either of the other two diets was considered to be of clinical importance.</p> <p>The data were analysed according to intention to treat.</p> <p>Mixed models were used to analyse the data. The models included a random effect for each person and assumed an underlying variance–covariance structure because of the multiple measures for each person. These provided appropriate standard errors for the statistical tests. Baseline measures were included to adjust for any baseline imbalance. The models examine relative change by setting the groups equal on the first occasion, and are the recommended way of overcoming problems associated with regression to the mean.</p> <p>Although the tests between the two alternative diets and the conventional diet were planned a priori, an overall test for all three diets was also carried out to compare the alternative diets. The value of the test statistic was compared with chi square distribution with appropriate degrees of freedom. The results are not reported in detail if the overall test was not statistically significant.</p>
Are the methods quantitative or qualitative?	Quantitative and qualitative
Safety Results	Observed increases in LDL cholesterol with the Atkins high- fat diet were less than expected. The LDL levels with the Atkins diet were significantly higher in the HF Atkins group than in the HP Zone group. The HF Atkins group produced a marked increase in LDL cholesterol in a small number of participants suggesting that some individuals may be particularly sensitive to substantial increases in fat intake.
Endpoint/ Biomarker Tested	Weight, waist circumference, BMI, blood lipids, blood pressure, glucose and insulin, C-reactive protein.
Are there end points other than those reported that might be relevant and important	Apo lipoprotein a and b, renal and bone health as one arm of the study was following the HF Atkins Diet.
Are the endpoints relevant to actual practice	Yes relevant to actual practice.
Dietary Intake and Adherence Results	<p>The reported energy intake did not differ between the three groups at any stage of the 6-month study.</p> <p>The high-fat Atkins (HF) group met the week 8 carbohydrate target. Those on the high-protein Zone (HP) diet did not meet the target protein and carbohydrate levels, as more energy was derived from total fat than intended.</p>

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Dietary Intake and Adherence Results contd.	<p>Those on the high-carbohydrate, high-fibre (HC) diet met the targets for total fat, but did not meet the targets for saturated fat, carbohydrates or fibre.</p> <p>Compared with the HC diet, the HF diet was much lower in carbohydrate (-94 g, 95% CI -112 to -75) and fibre (-8 g, 95% CI -10 to -6), and much higher in total fat (+40 g, 95% CI 29-52) and saturated fat (+17 g, 95% CI 12-22). The protein intake of the HP group was 20 g (95% CI 11-30) higher than that of the HC group. The HP diet was also higher in total fat, the increase due to higher intakes of both saturated and monounsaturated fatty acids in the HP group. The HP and HC groups had similar fibre intakes.</p> <p>Although there were some differences in micronutrient intake between the three groups (data not shown in report), these differences were small, and average intakes were above or close to recommended levels.</p>
Weight loss and cardio-protective and other mechanisms identified,	Reduced energy consumption due to novelty of a new diet, monotony due to restriction of accessible foods, enhanced satiety, and reduced appetite due to ketonuria associated with carbohydrate restriction.
<p>Weight Loss / Body Composition results</p> <p>Weight Loss / Body Composition results – Contd.</p>	<p>Body weight, waist circumference and triglycerides levels decreased with all three diets and the reductions were significantly greater in the HF and HP groups than in the HC group.</p> <p>Compared with the control (HC) group, those on the HF and the HP diets lost a significantly greater amount of weight.</p> <p>Similar between-group differences were observed for waist circumference and fat mass. Weight showed a significant time interaction.</p> <p>When compared with the HC group, body weight and BMI were reduced to a greater extent in the HF group than in the HP group at week 8. At week 16 the Atkins and Zone groups showed similar reductions. By week 24 the HP Zone group showed greater reductions than the HF Atkins group.</p> <p>When compared with the HC diet, the HF and HP diets were shown to produce significantly greater reductions in several parameters, including weight loss (Zone: -2.71, Atkins -2.82); , waist circumference (Zone: -2.66; Atkins -3.48) and fat mass (Zone: -1.64; Atkins: -1.64).</p>
Ketonuria Results	Not reported

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Cardiac Risk Factor Results	<p>When compared with the HC diet, the HF and HP diets were shown to produce significantly greater reductions in several parameters, including triglycerides (HF -0.30 mmol/l, HF -0.22 mmol/l). LDL cholesterol decreased in individuals on the HC and HP diets, but tended to fluctuate in those on the HF diet to the extent that overall levels were significantly lower in the HP group than in the HF group (-0.28 mmol/l, 95% CI 0.04–0.52, p=0.02). Of those on the HF diet, 25% showed a >10% increase in LDL cholesterol, whereas this occurred in only 13% of subjects on the HC diet and 3% of those on the HP diet.</p> <p>Fasting triglycerides, although reduced by all three diets, fell to a significantly greater extent with the HP and HF diets than with the HC diet.</p> <p>In accordance with a previous Study (Foster et al. 2003), the HF Atkins diet produced a small increase in HDL cholesterol which was similar to that observed for the HP Zone diet, but greater than that produced by the HC conventional diet.</p> <p>Overall, LDL cholesterol was lower in the HP group than in the HC group. Levels of LDL cholesterol were increased by >10% in eight individuals (25%) in the HF Atkins group, four (13%) in the HC group and one (3%) in the HP Zone group.</p> <p>Systolic and diastolic blood pressures were modestly reduced.</p> <p>Blood glucose levels (0 and 2 h), creatinine, liver enzymes, CRP and the albumin/creatinine ratio did not change throughout the observation period.</p> <p>Diastolic blood pressure was significantly lower in the HF group than in the HC group (-3 mm Hg, 95% CI -6 to 0, p=0.03).</p> <p>No significant differences were observed between the dietary groups with respect to systolic blood pressure, fasting and 2-h glucose, fasting insulin and CRP</p>
Endocrine markers and Hormonal Effects	<p>Insulin levels decreased with all three diets. This study suggests that the popular diets reduced insulin resistance to a greater extent than the standard dietary advice did. During the first 8 weeks of the study all three diets produced a decrease in fasting insulin levels that was maintained throughout the study period. The observed improvement in key indicators of insulin resistance (central adiposity, hyperinsulinaemia and hypertriglyceridaemia) confirms that insulin sensitivity was improved by all three dietary regimens.</p> <p>The greater reductions in waist circumference and triglycerides observed in the HF and HP groups indicate that insulin sensitivity may have been improved to a greater extent by the alternative diets than by the HC diet.</p> <p>Furthermore, only when HC diets are derived from intact vegetables and fruit and wholegrain cereals is the full potential benefit observed in terms of lipid profile and glycaemic control.</p> <p>In the present study, participants on the HC diet achieved only a modest increase in fibre density, and thus did not receive the maximum benefit of such a dietary regimen.</p>

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Exercise and Medication use	Not reported
What effect may bias have on the result?	None evident
The Author's conclusions - are these justified?	<p>The HF Atkins Diet is a successful short-term approach for weight loss; however, LDL levels should be monitored, and those who show a significant increase should be advised to discontinue the diet.</p> <p>The potential deleterious effects of the diet in the long-term remain a concern.</p> <p>In conclusion, in the context of this study the HP Zone Diet appears to be the most appropriate overall approach to reducing the risk of cardiovascular disease and type 2 diabetes. In routine practice a reduced-carbohydrate, higher protein diet may be the most appropriate overall approach to reducing the risk of cardiovascular disease and type 2 diabetes.</p>
Generalizability- the extent to which the results might apply outside the study	The use of restricted- carbohydrate diets for weight loss and the comparison to low-fat conventional diets is relevant outside the study.
Discussion points	<p>Compared with the HC diet, the HF Atkins and HP Zone diets produced greater reductions in weight. Although subjects on the two alternative diets lost a similar amount of weight, the initial weight loss appeared greater in the HF Atkins group, whereas later in the study the difference was reversed. This may be explained by the early fluid loss that occurs on a low-carbohydrate diet.</p> <p>Other studies comparing a single popular diet with the conventional approach have also reported that greater weight loss is achieved with HF and HP diets than with HC diets and there is much speculation regarding the mechanisms responsible for these findings. The majority of earlier studies in which macronutrient composition was altered against a background of constant energy intake reported no difference in weight change when HP or HF diets were compared with HC diets. Only when the diets were consumed <i>ad libitum</i> was a difference in weight loss apparent.</p> <p>It seems likely that greater weight losses observed when HF or HP alternatives are compared with HC diets (consumed without energy prescription) are the result of reduced energy consumption rather than the use of alternative fuel sources due to the altered macronutrient composition of the diets.</p> <p>Reduced energy intake on such diets may result from the novelty of a new diet, monotony due to restriction of accessible foods, or enhanced satiety or a reduced appetite due to the ketonuria that is associated with carbohydrate restriction.</p> <p>Although energy intake seemed to be restricted to a similar extent by all three diets in the present study, the results suggest that under-reporting took place.</p>

APPENDIX A8: Data Collection Sheets – McAuley et al. 2004.

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Discussion points – Contd.	<p>Three day diet records are not sensitive enough to detect small differences in energy intakes (of approximately 500 kJ/ day) which, over a period of months, could account for the observed differences in weight loss (about 3 kg) between the groups.</p> <p>Concern has been expressed regarding the long-term safety of HF diets, particularly the potential for such diets to elevate total and LDL cholesterol. In this study, the observed increases in these parameters were less than expected, probably due to the concomitant reduction in energy intake and weight loss.</p> <p>Although LDL levels were not markedly increased by the HF Atkins diet, levels were significantly higher in the HF Atkins group than in the HP Zone group, despite the fact that the two groups lost a similar amount of weight.</p> <p>Furthermore, the HF regimen produced a marked increase in LDL cholesterol in a small number of participants, suggesting that some individuals may be particularly sensitive to substantial increases in fat intake</p> <p>Fasting triglycerides were reduced by all three diets, but more so by the two popular diets. Fasting triglycerides decrease with weight loss, and carbohydrate-reduced diets have been reported to produce greater reductions than HC diets.</p> <p>The results of energy-controlled studies suggest that carbohydrate restriction may in itself result in lower triglyceride levels, however, these studies were of short duration, and did not allow for adaptation to a HC diet.</p> <p>During the first 8 weeks of the study all three diets produced a decrease in fasting insulin levels that was maintained throughout the study period. The observed improvement in key indicators of insulin resistance (central adiposity, hyperinsulinaemia and hypertriglyceridaemia) confirms that insulin sensitivity was improved by all three dietary regimens.</p> <p>The greater reductions in waist circumference and triglycerides observed in the HF and HP groups indicate that insulin sensitivity may have been improved to a greater extent by the alternative diets than by the HC diet.</p> <p>However, given that the aim in insulin resistant individuals is to reduce the cardiovascular risk as well as to reduce the risk of developing diabetes, the observed effect of the HF Atkins approach on LDL levels suggests that the HP diet offers a distinct advantage.</p> <p>Furthermore, a HF diet has been linked to other potentially deleterious effects not measured in the present study, including increased risk of thrombosis and cardiovascular disease associated with insufficient intake of wholegrain cereals. The data in this study does not indicate that any of the observed benefits afforded by the HF Atkins and HP Zone diets are a consequence of macronutrient composition; rather, they seem more likely to be secondary to the greater weight loss produced by these diets.</p>
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APPENDIX A8: Data Collection Sheets – McAuley et al. 2004.

(Text and/or data extracted verbatim from study article for many of the descriptive sections. Figure, Table and Numerical references included in brackets refer to the original article).

Discussion points – contd.	<p>The beneficial effects of the HP diet were achieved without full compliance. Protein and carbohydrate intakes in the HP group were lower than intended and fat intake was rather higher.</p> <p>Many participants did not achieve the required meal frequency. Thus, it would seem that the most frequent criticism of the Zone Diet—its rigid adherence to meal timing, is not an essential prerequisite to successful implementation.</p> <p>Those on the HC diet did not meet the targets for carbohydrate and fibre intakes, and saturated fatty acid intake remained higher than intended.</p> <p>It is probably necessary to be more directional with regard to fruit, vegetables and wholegrain cereals, which must be consumed in order to achieve targets. Given the high level of motivation of the volunteers, it seems likely that the guidelines employed to implement the HC recommendations were insufficiently specific.</p> <p>A diet that achieves the target carbohydrate and fibre levels (by increasing quantities of wholegrains, intact vegetables and fruits) would probably provide a benefit similar to that afforded by the HP approach.</p>
Were study limitations discussed?	<p>The HF Atkins diet has been linked to increased risk of thrombosis and CVD associated with insufficient intake of wholegrain cereals. These risks were not measured.</p> <p>The targets for carbohydrate and fibre intake were not met by the Conventional diet group and saturated fatty acid intake was higher than intended. Guidelines to high carbohydrate group were insufficiently specific</p>
Future Implications discussed	<p>Need to explore the potentially deleterious effects of the HF Atkins diet and the potential of the Zone diet for reducing CVD and diabetes.</p>

APPENDIX A9: Data Collection Sheets – Meckling et al. (2004)

(Text and/or data extracted verbatim from study article for many of the descriptive sections. Figure, Table and Numerical references included in brackets refer to the original article).

Author	Meckling, O'Sullivan & Saari (2004)
Title	Comparison of a Low-fat Diet to a Low-Carbohydrate Diet on Weight Loss, Body Composition and Risk Factors for Diabetes and Cardiovascular Disease in Free-Living, Overweight Men and Women.
Journal	The Journal of Clinical Endocrinology & Metabolism
Quality of Journal and competence of Researchers	Peer Reviewed Journal. The Principal author is a PhD associated with the Department of Human Biology and Nutritional Sciences, University of Guelph, Ontario, Canada.
General Aim Clear	To evaluate an energy restricted low-carbohydrate diet with an isocaloric conventional low-fat diet.
Specific Study objectives stated	<p>The authors had previously shown that in adult overweight women, a low-carbohydrate (LC) hypocaloric diet can promote efficient weight loss and improvements in body composition and lipid profile while maintaining glucose tolerance.</p> <p>The study was initiated to extend earlier observations made by the research team by directly comparing a conventional energy-restricted, low-fat (LF) diet to an equivalent energy-restricted LC diet in an overweight group of men and women.</p>
Aim and study objectives relevant to research question being explored External Validity - relevance of this particular piece of work to the issue under scrutiny	<p>Relevant to primary research question as to whether the macronutrient composition of a diet particularly carbohydrate restriction is significant to weight management and CVD risk management</p> <p>One non-ketogenic low-carbohydrate compared with a low-fat diet.</p>
Internal Validity - methods and actual results in the light of study objectives	Comparative Intervention.
Study described as randomised	Before initiation of the study, subjects were randomly assigned, on entry, to consume an energy-restricted, low-fat (LF) diet (control) or energy-restricted, LC diet for 10 weeks. There were no differences in the age, sex, weight, or BMI distribution between the two groups at randomization.
Study described as double blind	No
Description of withdrawals and dropouts present	Over the course of the study, four subjects dropped out of the LF group and five dropped out of the LC group (all female). Reasons for leaving the study included scheduling conflicts with blood collection, vacation plans, or noncompliance as evidenced at weekly counseling sessions and/or review of diet records.

APPENDIX A9: Data Collection Sheets – Meckling et al. (2004)

(Text and/or data extracted verbatim from study article for many of the descriptive sections. Figure, Table and Numerical references included in brackets refer to the original article).

Randomisation / blinding appropriate	To maintain objectivity, data concerning biochemical parameters were not un-blinded to identify subjects until after all samples had been analyzed. Blinding of the subjects to diet choice was not considered relevant.
Target Population	Overweight healthy Adults
Why was study done? What was perceived general importance?	To evaluate the effectiveness of a restricted-carbohydrate non-ketogenic diet where carbohydrates intake was at 50-70g /day.
Is there a clear hypothesis and objectives?	Not clearly stated but implied.
What specific question is being addressed?	Is a restricted carbohydrate diet at 50-70g/day as effective as an isocaloric low- fat conventional diet?
The study setting- where did study take place?	University of Guelph, Ontario Canada.
Group actually studied	Forty overweight, healthy adult volunteers (10 males and 30 females) were recruited from the Guelph community in Ontario, Canada via poster and newspaper advertisements between December 2000 and April 2001. There were initially 20 subjects enrolled in each experimental group; LF, 16 females, 4 males; LC, 15 females, 5 males.
The social, cultural, economic, ethnic background	Average age 42 years. No further details identified.
Study Approval	Approval for this study was granted by the Human Subjects Committee of the University of Guelph, and all subjects gave their informed, written consent to participate.
Was there clear inclusion and exclusion criteria and explanations of patient drop out?	Criteria for admission included a BMI of more than 25 with the potential for weight loss of 9 kg or more without becoming underweight (BMI < 20), sufficient energy intake as based on habitual diet (>4000 kJ/d), and strong personal motivation. Two subjects had BMIs close to the cutoff; however, both of these subjects had high body fat (>30%) as measured by bioelectrical impedance analysis (BIA) and thus were considered suitable weight loss subjects. Subjects were ineligible if they were on medications known to affect blood glucose, blood lipids, or blood pressure. Individuals with obesity secondary to clinically diagnosed endocrine disease were also excluded.
Is there a power calculation to determine sample size?	Not evident
Was there selection bias?	None evident
Was there funding bias?	Supported in part by the Natural Sciences Engineering Research Council of Canada
Confounding Factors	None Evident

APPENDIX A9: Data Collection Sheets – Meckling et al. (2004)

(Text and/or data extracted verbatim from study article for many of the descriptive sections. Figure, Table and Numerical references included in brackets refer to the original article).

How does the study group relate to researchers interest groups / patients?	Study group of overweight individuals within researcher's interest area.
What was the intervention and how was it carried out?	<p>Participants recorded at least 7 days of diet records before commencing the study diets. All study subjects were provided with journals, recipe ideas, information on how to keep accurate food records, and detailed food composition lists to assist with compliance.</p> <p>Subjects met weekly with one of the study coordinators for weight measurements and diet consultation.</p> <p>The goal of the LC diet was to restrict carbohydrates to 50–70 g/d. This was achieved by gradually restricting carbohydrate intake from 100 g on d 0 to 50–70 g by d 5. The restriction in carbohydrates resulted in concomitant energy restriction such that females achieved daily intakes of 5020–6690 kJ/d (1205-1605 kcal) and males 5860–9200 kJ/d (1406-2207 kcal).</p> <p>Subjects on the control diet (LF) were energy-restricted to achieve the same average energy restriction as the LC group.</p> <p>Subjects maintained detailed food diaries and exercise logs through the entire 10-wk period. Participants were instructed not to change their activity/exercise programs for the duration of the study.</p> <p>Food records were collected periodically, without prior announcement, throughout the 10-wk period to monitor compliance and ensure that energy intakes were similar between the two diet groups. Food records were analyzed using FoodWorks 3 (The Nutrition Company, Long Valley, NJ).</p> <p>When necessary, the intakes of LF subjects were adjusted through nutritional counseling to achieve matching energy intakes for the two experimental groups.</p> <p>Recommendations for food choices for the LC group included limiting intake of breads, pastas, rice, and desserts, eliminating intake of deep-fried foods, dried fruit, candy, sweetened soft drinks, and sugar and increased consumption of vegetables, lean meats, eggs, and nuts.</p> <p>Subjects on the LF regimen were instructed to eliminate high-fat dairy products and substitute with no-fat or LF alternatives, to increase intake of fruits, vegetables, whole-grain breads, and pastas and to eliminate fried foods, cream sauces, and high fat/sugar cakes, pastries, chocolate, and candy. They were also asked to reduce use of oil products in cooking.</p> <p>As with LC subjects, LF subjects were encouraged to consume lean meats as alternatives to high-fat meat products.</p> <p>Weekly counseling sessions were held to instruct subjects in both groups on appropriate dietary choices to meet the energy and fat or carbohydrate restriction.</p>

APPENDIX A9: Data Collection Sheets – Meckling et al. (2004)

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What was measured and how was it measured?	<p>Weight was measured weekly, in similar clothing without shoes, to the nearest quarter kilogram using an electronic scale and tape measure to estimate the subjects' weight (kilograms) and height (centimeters) respectively.</p> <p>Blood pressure was measured while the subject was sitting in a chair after a 5-min rest period, using a digital, self-inflating cuff. Measurements were taken in duplicate and averaged. Hypertension was defined as systolic blood pressure more than 140 mm Hg and/or diastolic pressure 90 mm Hg or more.</p> <p>Body composition was estimated at baseline, wk 6, and wk 10 by BIA (Bodystat 1500; Bodystat, Inc., Tampa, FL).</p> <p>To decrease dehydration, which could complicate the BIA measures, subjects were instructed to refrain from consumption of alcohol and caffeine and to avoid exhaustive exercise 24 h before the measurements were to take place. Subjects were encouraged to take in as much water as possible in the 2 d leading up to the measurements, and all subjects attempted to void immediately before the BIA.</p> <p>Total cholesterol, HDL cholesterol, triglycerides were also measured. Glucose was analyzed. Plasma insulin was measured at baseline and 10 wk. PAI-1 functional enzyme activity was measured by bioimmunoassay. D(-)3-hydroxybutyrate, the assay of Ketones were assessed.</p>
Were baseline measures used?	Baseline characteristics of the two experimental groups were comparable in terms of sex distribution, age, weight, height, and BMI.
Were process measures used?	The average intake over at least a 7-d consecutive period was used for each subject at two time points during the 10-wk study, in addition to habitual intake before study entry.
Were outcome measures identified? Are there clear validated outcomes?	Weight, BP, body composition, lipids, Glucose, Insulin, β -Hydroxybutyrate
Are the methods quantitative or qualitative?	Both quantitative and qualitative
Safety Results	No subjects reported significant side effects in either treatment group.
Endpoint/ Biomarker Tested	Weight, BP, body composition-BMI , lipids, Glucose, Insulin, B-Hydroxybutyrate, Micronutrients

APPENDIX A9: Data Collection Sheets – Meckling et al. (2004)

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Are there other end points other than those reported that might be relevant and important	Apo lipoprotein a and b.
Are the endpoints relevant to actual practice	Yes and consistent with other studies.
Dietary Intake and Adherence Results	<p>The average energy restriction over the 10-wk protocol was 2540 kJ (606 kcal) for the LF group and 3195 kJ (763 kcal) for the LC group.</p> <p>Although total protein intake (grams) did not change for subjects on the LC diet, because total energy decreased there was a net increase in the proportion of energy coming from protein in this group. Changes in protein intake were not significant for the LF group, and the LF group did not differ from the LC group at either baseline or after the 10-wk intervention period.</p> <p>Total fat intake did not change for subjects on the LC group but for LF subjects decreased by approximately 50 g/d producing a decrease in the percentage of energy from a habitual diet of 36.4% to an average of 17.8%. LF subjects consumed lower levels of all three classes of fatty acids and cholesterol compared with their habitual diets. The LC group consumed similar levels of fatty acids to their habitual diets but also consumed 250 mg of additional cholesterol not seen in their habitual diets.</p> <p>The largest dietary change for the LC group was a substantial decrease in carbohydrate intake by 228 g/d. This decrease included both complex carbohydrates as well as simple sugars. In contrast, there was a significant increase in carbohydrate consumption by the LF group (+13 g/d).</p> <p>The decrease in carbohydrate-rich foods was associated with a 50% decrease in fiber intake on the LC diet.</p> <p>Micronutrient Status Common changes in intake between the LF and LC protocols included a decrease in daily calcium (LF, -147 mg/d; LC, -139 mg/d), decrease in daily sodium (LF, -728 mg/d; LC, -1095 mg/d), and decrease in daily riboflavin (LF, -0.4 mg/d; LC, -0.9 mg/d) intake. Changes unique to the LF diet were a decrease in vitamin E (-2.2 mg/d) and an increase in vitamin C (+38 mg/d). Habitual folate intakes were higher in the LC group than the LF group, which resulted in a significant decrease in folate intake for the LC group on the intervention diet</p> <p>Other dietary intake changes unique to the LC diet included: lower potassium (-1050 mg/d), lower iron (-7 mg/d), lower magnesium (-77 mg/d), lower vitamin C (-82 mg/d), lower vitamin D (-64 mg/d), lower thiamin (-0.9 mg/d), lower vitamin B6 (-1.0 mg/d), and an approximate doubling of vitamin K intake (+41 µg/d).</p>

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Weight loss and cardioprotective mechanisms identified	<p>For both the LC and the LF diets, there was an energy deficiency in relation to habitual intake</p> <p>LC Approach showed significant decrease in circulating insulin that translated to a significant decrease in insulin to glucose ratio, a possible indicator of insulin sensitivity.</p> <p>PAI-1 levels decreased in both groups which correlated with circulating triglycerides suggesting a reduction of CVD risk.</p>
Weight Loss / Body Composition results	<p>BMI decreased by approximately 2 kg/m² with both control (LF) and test (LC) diet interventions.</p> <p>Total body weight decreased by 6.8 kg in the LF group and by 7.0 kg in the LC group over the 10-wk period.</p> <p>There was no difference in the pattern of weight loss over time between the two groups.</p> <p>Significant losses in fat weight were observed in both groups (LF, -5.4 kg; LC, -4.1 kg), but a significant decrease in lean mass (-1.9 kg) was observed only in subjects on the LC diet.</p>
Cardiac Risk Factor Results	<p>Twelve of 31 subjects completing all 10wk of the study had some form of abnormal blood pressure at baseline. The group results indicated that both diets were equally effective in reducing systolic blood pressure by about 10 mm Hg and diastolic blood pressure by 5 mm Hg.</p> <p>PAI-1 bioactivity, as a risk factor for cardiovascular disease was similar in both groups of subjects at baseline and significant improvements were observed for both groups after 10 wk of diet intervention.</p> <p>The magnitude of the decrease in PAI-1 appeared larger for the LF group, but this was not statistically different from the change observed in the LC group.</p> <p>Total cholesterol values at baseline indicated that six subjects in each diet category had hypercholesterolemia (>6.2 mm) and six more had borderline hypercholesterolemia (5.2–6.2 mm). After 10 wk, significant improvements in total cholesterol values were only observed in the LF group.</p> <p>Group results indicated that total and LDL cholesterol levels were unchanged from baseline in LC subjects, whereas total cholesterol decreased by 1.6 mm. LDL cholesterol decreased by 1.3 mm in LF subjects.</p> <p>LF subjects also showed a significant decrease (-0.3 mm) in HDL cholesterol. LC subjects showed a significant increase (+0.14) in HDL cholesterol.</p>

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Cardiac Risk Factor Results – Contd.	<p>Group results indicated that both LC and LF groups saw a decrease of 0.4 mm in total triglyceride values over the intervention period.</p> <p>There was an increase in circulating β hydroxybutyrate at the 2- and 4-wk time points in the LC group that remained numerically higher for the remainder of the study but not statistically different from the high at 2–4 wk or baseline.</p> <p>There were no statistical differences between the LC and LF subjects after wk 4.</p> <p>There was no change in β-hydroxybutyrate concentration over time in the LF group.</p>
Endocrine markers and Hormonal Effects	<p>Although individual results suggested some improvements in glucose control, group results indicated that there was no significant decrease in fasting serum glucose or either LF or LC interventions.</p> <p>However, fasting insulin levels were significantly lower after 10 wk of the LC diet, but not the LF diet.</p> <p>Nine subjects (seven in the LC group and two in the LF group), by definition, had impaired fasting glucose (>6.1 mm) at baseline and at least one other time point in the study. In fact, five of these individuals would be diagnosed as type II diabetic (>7.0mm) using fasting plasma glucose as the lone indicator. This resulted in a significant decrease in the insulin to glucose ratio for the LC group after diet intervention.</p> <p>There was no change in fasting glucose or insulin to glucose ratio for the LF subjects.</p>
Exercise and Medication use	Participants were instructed not to change their activity /exercise programs for the duration of the study and Subjects maintained detailed exercise logs through the entire ten week period.
What effect may bias have on the result?	None evident
The Author's conclusions - are these justified?	<p>Hypoenergetic diets of widely differing macronutrient concentration are feasible strategies for promoting short-term weight loss and improvements in chronic disease risk markers in overweight and obese men and women.</p> <p>A LF regimen may be preferred when reduction of blood cholesterol is a primary goal, whereas the LC regimen may be more appropriate when improvement in insulin sensitivity is the target.</p> <p>Either strategy promotes loss of fat weight and improvements of similar magnitude in blood pressure, and triglycerides, both of which can be seen as additional benefits to chronic disease risk reduction in addition to weight loss itself.</p>

APPENDIX A9: Data Collection Sheets – Meckling et al. (2004)

(Text and/or data extracted verbatim from study article for many of the descriptive sections. Figure, Table and Numerical references included in brackets refer to the original article).

Generalizability- the extent to which the results might apply outside the study	These results may be applied outside the study and remains relevant for short- term weight loss and improvement of CVD risk factors.
Discussion points	<p>The outcomes in our study population suggest that either a LF or a LC energy-restricted diet is an effective means for short-term weight loss in overweight adults.</p> <p>Dietary compliance was assessed by interview and diet records and for the LC correlated well with early rises in blood β-hydroxybutyrate.</p> <p>Energy restriction alone predicted a weight loss of 5.5. and 6.9 kg, respectively, in the LF and LC groups, which was close to the observed values of 6.8 and 7 kg for the same groups.</p> <p>Slight differences, particularly for LF subjects might be explained by underreporting of habitual diets, as the subjects became better able to estimate their intakes and keep better food records as the trial proceeded.</p> <p>BMI was improved in both groups of subjects and this was largely attributed to a decrease in fat mass.</p> <p>Although both groups also experienced losses in lean mass, this was only significant in the LC group, suggesting that a LF diet regimen with sufficient protein may better preserve lean mass.</p> <p>The study suggests that changes in LDL cholesterol may be transient. The LF diet used was less than 18% fat energy, which is considerably lower than the LF diets reported by others where increases in triglycerides were sometimes reported. The very LF level may also be responsible for the decrease in HDL cholesterol seen in this study and similar to the results of other LF diet intervention studies.</p> <p>This suggests that despite a slight decrease in HDL cholesterol in this group, the ratios of total cholesterol and LDL cholesterol to HDL cholesterol were all improved in both diet groups as was the ratio of triglyceride to HDL cholesterol, all indicators of cardiovascular disease risk reduction.</p> <p>Factors other than macronutrient composition must dominate in determining circulating triglyceride levels because the LC and LF differed so extremely in macronutrient content and yet resulted in identical triglyceride changes.</p> <p>In addition to being energy deficient relative to habitual diets, both the LF and LC diet restrictions resulted in major changes in micronutrient intake.</p> <p>In the short term, decreases in sodium intake may contribute to the improvements in blood pressure observed in both diet groups. If either of these diet patterns were to be pursued in the longer term, issues of calcium and vitamin E nutrition could become important in the LF regimen and calcium, magnesium, iron, vitamin D, folate, and B6 intakes relevant to those consuming a very LC diet.</p>

APPENDIX A9: Data Collection Sheets – Meckling et al. (2004)

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Discussion points – Contd.	<p>Dietary inadequacy can be tolerated in the short term to achieve weight loss goals, but maintenance diets must include the right balance of micronutrients to promote optimal health.</p> <p>Thus, the long-term impacts of these diet strategies on biochemical parameters and markers of disease risk need to be evaluated.</p> <p>With respect to glucose control, there were no significant changes in the LF group; however, on an individual basis, there were a number of subjects whose fasting glucose values improved over the study period. Mean insulin values were in the normal range for both diet groups at baseline and after 10 wk of intervention. Only the LC group showed a significant decrease in circulating insulin that translated into a significant decrease in insulin to glucose ratio, a possible indicator of insulin sensitivity. The more severe the insulin resistance (high insulin and high glucose), the more likely the subjects are to benefit from weight loss.</p> <p>The PAI-1 levels decreased in both diet groups, which would predict a reduction cardiovascular disease risk.</p> <p>The only blood marker that correlated with PAI-1 in the current study (regardless of diet group) was circulating triglyceride levels consistent with what other researchers have found.</p>
Were study limitations discussed?	<p>Data for waist circumference was not taken hence estimates for metabolic syndrome and those at high risk are underestimates of the real frequency in this population. Thus despite subjects' belief that they were overweight/obese but otherwise healthy- this was inaccurate.</p>
Future Implications discussed	<p>Better screening of Adults to prevent diabetes type II, CVD and the metabolic syndrome and to promote early dietary and physical activity interventions is needed.</p>

APPENDIX A10: Data Collection Sheets- Parker et al. 2002

(Some sections of text and/or data extracted verbatim from the reference paper. Figure, Table and Numerical references included in brackets refer to the original article).

Author	Parker, Luscombe, Noakes & Clifton (2002)
Title	Effect of a High-Protein, High- Monounsaturated Fat Weight Loss Diet on Glycemic Control and Lipid Levels in Type 2 Diabetes
Journal	Diabetes Care
Quality of Journal and competence of Researchers	Peer Reviewed Journal. Two authors are Phds and two are BScs.
General Aim Clear	Assessing the effects of a high protein (HP) weight loss diet compared with a lower protein (LP) on fat and lean tissue and fasting and postprandial glucose and insulin concentrations. Replacing dietary protein for carbohydrate (CHO) during energy restriction and weight loss has been effective in sparing lean mass and improving insulin sensitivity in obese subjects but has not been tested in subjects with type 2 diabetes.
Specific Study objectives stated	To compare a HP diet – 28% Protein, 42% CHO, 28% Fat with 8% Saturated Fat, 12% monounsaturated FA and 5% PUFA with a LP Diet – 16% Protein, 55% CHO, 26% Fat with 8% saturated fat, 11% MUFA, 5% PUFA in 54 obese men and women with T2D during 8 weeks of energy restriction (1600 kcals) and 4 weeks of energy balance .
Aim and study objectives relevant to research question being explored External Validity - relevance of this particular piece of work to the issue under scrutiny	Relevant to primary research question as to whether the macronutrient composition of a diet is significant to weight management and CVD risk management. A moderate-carbohydrate Zone type Diet compared with a higher-carbohydrate conventional diet.
Internal Validity - methods and actual results in the light of study objectives	Comparison of 2 diets – effect on body composition measured via DEXA at weeks 0 and 12.
Study described as randomised	No but subjects were randomly assigned to the two diets.
Study described as double blind	No
Description of withdrawals and dropouts present	Yes. Of 66 subjects recruited, 54 completed the study. 2 subjects withdrew before commencement. A further 10 subjects, 5 from each group withdrew throughout the study.
Randomisation / blinding appropriate	Randomisation appropriate.
Target Population	Type 2 Diabetics

APPENDIX A11: Data Collection Sheets – Sacks et al. (2009)

(Text and/or data extracted verbatim from study article for many of the descriptive sections. Figure, Table and Numerical references included in brackets refer to the original article).

Author	Sacks et al. (2009)
Title	Comparison of Weight-Loss Diets with Different Compositions of Fat, Protein, and Carbohydrates
Journal	The New England Journal of Medicine
Quality of Journal and competence of Researchers	Peer Reviewed Journal. 17 Authors listed – 5 of whom are MDs and 6 are PhDs. FM Sacks is a member of the Department of Nutrition. Harvard School of Public Health
General Aim Clear	To assess the significance of the macronutrients on weight loss over one year. The crucial question is whether overweight people have a better response in the long term to diets that emphasize a specific macronutrient composition.
Specific Study objectives stated	To compare the effects of three principal dietary macronutrients over two years, recognizing that weight loss typically is greatest 6-12 months after initiation of the diet with steady regain of weight subsequently.
Aim and study objectives relevant to research question being explored External Validity - relevance of this particular piece of work to the issue under scrutiny	Relevant to primary research question as to whether the macronutrient composition of a diet is significant to weight management and cardiovascular disease (CVD) risk management. Two lower-carbohydrate diet plans where carbohydrate was 35% and 45 % of energy similar to the Zone type diet compared with 2 diets with a low-fat/higher carbohydrate design.
Internal Validity - methods and actual results in the light of study objectives	Randomized , comparative intervention
Study described as randomised	Yes 811 overweight adults randomly assigned to one of 4 diets. The targeted percentages of energy from fat, protein and carbohydrates (CHO) in the four diets.
Study described as double blind	No
Description of withdrawals and dropouts present	Of 1638 participants who were screened, 811 (50%) were randomly assigned to a diet, and 645 (80% of those assigned) completed the study (i.e., provided a body-weight measurement at 2 years) Detailed description of dropouts and participants are available in the supplementary index. Of 201 allocated to HF/HP (40%F:25%P:35%Carb), 168 completed; 6 withdrew, 27 lost to follow up of which 19 did not respond to repeated contact, 2 missed scheduled appointment, 1 moved away.

APPENDIX A11: Data Collection Sheets – Sacks et al. (2009)

(Text and/or data extracted verbatim from study article for many of the descriptive sections. Figure, Table and Numerical references included in brackets refer to the original article).

Description of withdrawals and dropouts present contd.	<p>Of 204 allocated to HF/AP (40% Fat, 15% Protein, 45% Carb), 151 completed, 12 withdrew, 41 lost to follow up.</p> <p>Of 202 allocated to LF/HP (20%F:25%P:55% C), 157 completed, 11 withdrew and 34 lost to follow up</p> <p>Of 204 allocated to LF/AP (20%Fat:15%P:65%C) 169 completed, 7 withdrew and 28 were lost to follow up of which 2 moved away, 20 did not respond and 6 did not meet scheduled appointment.</p>
Randomisation / blinding appropriate	<p>Blinding was maintained by use of similar foods for each diet.</p> <p>Staff and participants were advised that each diet adhered to principles of a healthful diet and recommended for long term weight loss thereby establishing equipoise. Staff who measured outcomes were unaware of the diet assignment of the participants.</p>
Target Population	Overweight and obese 30-70 year old Adult Subjects
Why was study done? What was perceived general importance?	<p>To conduct a large trial designed to overcome limitations of previous trials comparing the effects of the three macronutrients. Limitations noted were small samples, underrepresentation of men, limited generalizability, a lack of blinded ascertainment of the outcome, a lack of data on adherence to assigned diets and a large loss to follow up.</p> <p>Weight loss studied over course of 2 years to evaluate the weight loss, weight regain and plateaux phases.</p>
Is there a clear hypothesis and objectives?	Not clearly stated but implied hypothesis relates to the importance of macronutrient levels for weight management.
What specific question is being addressed?	Whether macronutrient composition affects weight management.
The study setting- where did study take place?	Trial conducted at 2 sites: The Harvard School of Public Health and Brigham and Women's Hospital Boston; and the Pennington Biomedical Research Centre of the Louisiana State University
Group actually studied	Overweight and obese generally healthy adults ensuring the inclusion of adequate number of male subjects
The social, cultural, economic, ethnic background	Overweight and obese subjects of which 40% would be men.
Study Approval	The study was approved by the National Heart Lung and Blood Institute.
Was there clear inclusion and exclusion criteria and explanations of patient drop out?	<p>Inclusion criteria: Participants had to be 30-70 years of age and have a body mass index of 25-40.</p> <p>Exclusion Criteria: presence of Diabetes treated with oral medications or insulin or unstable CVD; use of medication that affects body weight and insufficient motivation as assessed by interview and questionnaire.</p>

APPENDIX A11: Data Collection Sheets – Sacks et al. (2009)

(Text and/or data extracted verbatim from study article for many of the descriptive sections. Figure, Table and Numerical references included in brackets refer to the original article).

Is there a power calculation to determine sample size?	The study was powered to detect a 1.67-kg weight loss as an effect of the level of protein or fat in the diet over the 2-year period, assuming a withdrawal rate of 40%.
Was there selection bias?	Not evident.
Was there funding bias?	None evident. The study was supported by grants from the National, Heart, Lung and Blood Institute.
Confounding Factors	None noted.
How does the study group relate to researchers interest groups / patients?	The researcher's interest groups would potentially include overweight and/or obese adults
What was the intervention and how was it carried out?	<p>The nutrient goals for the 4 diet groups. 20% fat, 15% protein and 65% carbohydrates (CHO) the low-fat average-protein plan(LFAP); 20% fat, 25% protein and 55% CHO the low fat, high protein plan (LFHP); 40% fat, 15% protein and 45% CHO- the high fat, average protein plan (HFAP); and the 40% fat, 25% protein and 35% CHO- the high fat, high-protein plan (HFHP).</p> <p>Design: 2 by 2 factorial design and allowed a dose response test of CHO intake that ranged from 35 to 65% of energy.</p> <p>Other goals for all groups were that diets should include 8% or less of saturated fat, at least 20g of dietary fibre and 150mg or less of cholesterol per 1000kcal. Carbohydrate rich foods with a low glycemic index were recommended in each diet.</p> <p>Each person had a caloric prescription of a 750 kcal deficit per day from baseline as calculated from the participant's resting energy expenditure and activity level. No initial diet had less than 1200kcal/d.</p> <p>Group sessions were held once a week, 3 of every 4 weeks during the first six months and 2 of every 4 weeks from 6 months to 2 years. Individual sessions were held every 8 weeks for entire two years.</p> <p>Daily meal plans in 2-week blocks were provided.</p> <p>Participants were instructed to record their food and beverage intake in a daily food diary in a web based self-monitoring tool. Behavioural counselling was integrated to promote adherence to the assigned diets.</p> <p>Contact among the groups was avoided.</p> <p>The goal for physical activity was 90 minutes per week.</p> <p>Participation in exercise was monitored by questionnaire and by an online self-monitoring tool.</p>

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<p>What was measured and how was it measured?</p>	<p>Body weight and waist circumference were measured in the morning before breakfast on 2 days at baseline, 6 months, and 2 years, and on a single day at 12 and 18 months.</p> <p>Dietary intake was assessed in a random sample of 50% of the participants, by a review of the 5-day diet record at baseline and by 24-hour recall during a telephone interview on 3 non-consecutive days at 6 months and at 2 years.</p> <p>Questionnaires that asked for information on satiety, food craving, eating behaviour, and satisfaction with the diet were administered at baseline (except for diet satisfaction) and at 6 months and 2 years.</p> <p>Fasting blood samples, 24-hour urine samples, and measurement of resting metabolic rate were obtained on 1 day, and blood-pressure measurement on 2 days, at baseline, 6 months, and 2 years.</p> <p>Levels of serum lipids, glucose, insulin, and glycated haemoglobin were measured at the clinical laboratory at the Pennington Biomedical Research Centre.</p> <p>Blood pressure was measured with the use of an automated device (HEM-907XL, Omron). The participants were evaluated for the presence of the metabolic syndrome, which was defined by the presence of at least three of the following five criteria: waist circumference of more than 102 cm in men or more than 88 cm in women, a triglyceride level of 150 mg per deciliter (1.69 mmol per litre) or more, a high density lipoprotein (HDL) cholesterol level of less than 40 mg per deciliter (1.03 mmol per litre) in men or less than 50 mg per deciliter (1.29 mmol per litre) in women, a blood pressure of 130/85 mm Hg or more, and a fasting glucose level of 110 mg per deciliter (6.1 mmol per litre) or more.</p>
<p>Were baseline measures used?</p>	<p>Baseline characteristics were similar among participants assigned to the four diets and between those who were assigned to a diet and those who completed the study.</p>
<p>Were process measures used?</p>	<p>Statistical Analysis</p> <p>Data were pooled from the diets for the two factorial comparisons: low fat versus high fat and average protein versus high protein. The analysis also included a comparison of two of the four diets, the diet with the lowest carbohydrate content and the diet with the highest carbohydrate content, and included a test for trend across the four levels of carbohydrates.</p> <p>The effects of protein, fat, and carbohydrate levels were evaluated independently with the use of two-sample t-tests at a two-sided significance level of 0.05.</p> <p>Exploratory post hoc analyses were performed with threshold amounts of weight loss as outcomes, with Bonferroni's adjustment for multiple comparisons.</p> <p>Associations between adherence to the fat and protein goals and weight loss were also explored in post hoc analyses.</p> <p>An intention-to-treat analysis was performed in which long-term weight loss for persons who withdrew from the study early (after at</p>

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Were process measures used? contd.	<p>least 6 months of participation) was imputed on the basis of a rate of 0.3 kg per month of regained weight and a rate of 0.3 cm per month of regained waist circumference after withdrawal.</p> <p>Risk factors for cardiovascular disease and diabetes were also analyzed according to the intention-to-treat principle, with zero change from baseline imputed for missing data.</p>
Were outcome measures identified? Are there clear validated outcomes?	Yes
Are the methods quantitative or qualitative?	Both quantitative and qualitative
Safety Results	<p>Adverse events were reported by 57 participants (7%); there were no significant differences in the rates among diets.</p> <p>The ratio of urinary microalbumin to creatinine was more than 30 in five participants in the average-protein group and in five participants in the high-protein group at 6 months and in seven participants, all in the average protein groups, at 2 years.</p> <p>There was a larger decrease in urinary nitrogen excretion from baseline in the average-protein group than in the high protein group (a difference in the change of 1.6 g at 6 months and 0.8 g at 2 years. These differences correspond to a difference in dietary protein of 10 g per day and 5 g per day, respectively.</p>
Endpoint/ Biomarker Tested	The primary outcome of the study was the change in body weight over a period of 2 years, and the secondary outcome was the change in waist circumference
Are there end points other than those reported that might be relevant and important	Apo lipoprotein a and b
Are the endpoints relevant to actual practice	Yes
Dietary Intake and Adherence Results	<p>Mean reported intakes at 6 months and 2 years did not reach the target levels for macronutrients. The reported intakes represented differences from target levels of fat, protein, and carbohydrate intake of 8.0, 4.2, and 14.4 percentage points, respectively, at 6 months and 6.7, 1.4, and 10.2 percentage points, respectively, at 2 years.</p> <p>Reported energy intakes and physical activity were similar among the diet groups.</p> <p>The participants who completed the study had a mean weight loss of 6.5 kg at 6 months, which corresponds to a reduction in daily energy intake of approximately 225 kcal.</p> <p>The respiratory quotient was 0.84 at baseline in both the high-fat and low-fat groups, and the between-group difference in the</p>

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<p>Dietary Intake and Adherence Results contd.</p>	<p>change at 2 years (the value in the high-fat group minus the value in the low-fat group) was -0.02 ($P = 0.002$).</p> <p>Thus, changes in biomarkers confirmed that differences among the groups in macronutrient intake were consistent with those recorded in the dietary reports and that participants modified their intake of macronutrients in the direction of the goals, although the targets were not fully achieved.</p> <p>Adherence to the goal for protein intake was associated with more weight loss only in the high protein groups, and adherence to the goal for fat intake was associated with more weight loss only in the low-fat groups ($P < 0.001$).</p>
<p>Weight loss and cardio-protective and other mechanisms identified,</p>	<p>Craving, fullness, and hunger and diet-satisfaction scores were similar at 6 months and at 2 years among the diets.</p> <p>Attendance at group sessions strongly predicted weight loss at 2 years (0.2 kg for every session attended) and was similar among the diet groups</p>
<p>Weight Loss / Body Composition results</p>	<p>Weight Loss At 6 months, participants assigned to each diet had lost an average of 6 kg, which represented 7% of their initial weight; they began to regain weight after 12 months.</p> <p>By 2 years, weight loss remained similar in those who were assigned to a diet with 15% protein and those assigned to a diet with 25% protein (3.0 and 3.6 kg, respectively); in those assigned to a diet with 20% fat and those assigned to a diet with 40% fat (3.3 kg for both groups); and in those assigned to a diet with 65% carbohydrates and those assigned to a diet with 35% carbohydrates (2.9 and 3.4 kg, respectively) ($P > 0.20$ for all comparisons). Among the 80% of participants who completed the trial, the average weight loss was 4 kg; 14 to 15% of the participants had a reduction of at least 10% of their initial body weight.</p> <p>Satiety, hunger, satisfaction with the diet, and attendance at group sessions were similar for all diets; attendance was strongly associated with weight loss (0.2 kg per session attended).</p> <p>The change in waist circumference did not differ significantly among the diet groups.</p> <p>Most of the weight loss occurred in the first 6 months. Changes from baseline differed among the diet groups by less than 0.5 kg of body weight and 0.5 cm of waist circumference.</p> <p>After 12 months, all groups, on average, slowly regained body weight. A total of 185 of the participants (23%) continued to lose weight from 6 months to 2 years. The mean (\pmSD) additional weight loss was 3.6 ± 3.5 kg, for a mean total loss from baseline of 9.3 ± 8.2 kg, with no significant differences among the diet groups.</p> <p>At 2 years, 31 to 37% of the participants had lost at least 5% of their initial body weight, 14 to 15% of the participants in each diet</p>

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Weight Loss / Body Composition results – Contd.	group had lost at least 10% of their initial weight, and 2 to 4% had lost 20 kg or more (P>0.20 for the comparisons between diets).
Cardiac Risk Factor Results	<p>All the diets reduced risk factors for cardiovascular disease and diabetes at 6 months and 2 years.</p> <p>At 2 years, the two low-fat diets and the highest-carbohydrate diet decreased low-density lipoprotein cholesterol levels more than did the high-fat diets or the lowest-carbohydrate diet (low-fat vs. high-fat, 5% vs. 1% [P = 0.001]; highest carbohydrate vs. lowest-carbohydrate, 6% vs. 1% [P = 0.01]).</p> <p>The lowest-carbohydrate diet increased HDL cholesterol levels more than the highest-carbohydrate diet (9% vs. 6%, P = 0.02). There was a larger increase from baseline in the HDL cholesterol level, a biomarker for dietary carbohydrate, in the lowest-carbohydrate group than in the highest-carbohydrate group (a difference in the change of 2 mg per deciliter at 2 years). This difference corresponds to a predicted difference in carbohydrate intake of 6%.</p> <p>All the diets decreased triglyceride levels similarly, by 12 to 17%.</p> <p>Blood pressure decreased from baseline by 1 to 2 mm Hg, with no significant differences among the groups (P>0.59 for all comparisons).</p> <p>These changes in risk factors in the intention-to-treat population were about 30 to 40% smaller than the changes seen among participants who provided data at 2 years, reflecting the effect of the imputation of missing values</p>
Endocrine markers and Hormonal Effects	<p>All the diets except the one with the highest carbohydrate content decreased fasting serum insulin levels by 6 to 12%; the decrease was larger with the high-protein diet than with the average-protein diet (10% vs. 4%, P = 0.07).</p> <p>The metabolic syndrome was present in 32% of the participants at baseline, and the percentage was lower at 2 years, ranging from 19 to 22% in the four diet groups (P = 0.81 for the four-way comparison).</p>
Exercise and Medication use	<p>Physical Activity goals were established for sedentary participants gradually increasing from 30 minutes of moderate intensity per week to 90 minutes per week during first 6 months Participants were encouraged to do more if they could. Minutes of exercise were monitored using self-monitoring forms.</p> <p>Reported physical activity was similar among the diet groups.</p>
What effect may bias have on the result?	None evident

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The Author's conclusions - are these justified?	Diets that are successful in causing weight loss can emphasize a range of fat, protein, and carbohydrate compositions that have beneficial effects on risk factors for cardiovascular disease and diabetes. Such diets can also be tailored to individual patients on the basis of their personal and cultural preferences and may therefore have the best chance for long-term success.
Generalizability- the extent to which the results might apply outside the study	The four different dietary strategies representing differing percentages of various macronutrients provide clinical options to consider when making dietary recommendations.
Discussion points	<p>The principal finding is that the diets were equally successful in promoting clinically meaningful weight loss and the maintenance of weight loss over the course of 2 years.</p> <p>Satiety, hunger, satisfaction with the diet, and attendance at group sessions were similar for all diets.</p> <p>The diets improved lipid risk factors and fasting insulin levels in the directions that would be expected on the basis of macronutrient content.</p> <p>The study had a large sample, a high rate of retention, and the sensitivity to detect small changes in weight.</p> <p>The findings should be directly applicable to both clinicians' recommendations for weight loss in individual patients and the development of population-wide recommendations by public health officials.</p> <p>Despite the intensive behavioural counselling in the study, participants had difficulty achieving the goals for macronutrient intake of their assigned group. The mean differences among the groups in fat, carbohydrate, or protein intake at 6 months were nevertheless often greater than those in several previous trials comparing diets for weight loss.</p> <p>Substantially diminished adherence after the first few months is typical in weight loss trials and occurred between 6 months and 2 years in our trial.</p> <p>Only two trials have reported dietary intake beyond 1 year and one of them provided foods to the participants.</p> <p>In addition, trials of low-carbohydrate diets have reported a very low incidence of urinary ketosis after 6 months suggesting that in most overweight people, it is futile to sustain a low intake of carbohydrates.</p> <p>Overall, these findings with respect to adherence to macronutrient goals suggest that participants in weight-loss programs revert to their customary macronutrient intakes over time but may nonetheless be able to maintain weight loss.</p> <p>Attendance had a strong association with weight loss, and the association was similar across diet groups. The Authors view attendance at counselling sessions as a proxy for commitment to achieving weight loss.</p>

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Discussion points – contd.	<p>Study participants who attended two thirds of the sessions over the course of 2 years lost about 9 kg of weight.</p> <p>Regain after 6 to 12 months was about 20% of the regain reported in earlier trials. Several recent trials have also shown that continued contact with participants after weight loss is associated with less regain. These findings together point to behavioural factors rather than macronutrient metabolism as the main influences on weight loss.</p> <p>The authors used a generic approach to developing each diet and the instructions for following it, in order to minimize Influences media attention, cultural norms or scientific novelty.</p> <p>No diet was considered to be a control diet, and the dietary counselling and the attention that we provided were the same for all diet groups throughout the study period.</p> <p>The authors did not confirm previous findings that low-carbohydrate or high protein diets caused increased weight loss at 6 months and that the advantage of these diets usually eroded by 12 months, with weight loss that was nearly or fully equivalent to that with low-fat diets.</p> <p>Other studies showed increased weight loss at 1 to 2 years with diets that were high in unsaturated fat or with low-fat, high-carbohydrate vegetarian diets.</p> <p>When non nutritional influences are minimized, as they were in this study, the specific macronutrient content is of minor importance as was suggested many years ago.</p>
Were study limitations discussed?	<p>Association of achieved nutrition with weight loss explored. These post hoc analyses do not have the strong validity of the main analysis which compared randomized groups. Protein and fat intakes overlapped hence confounding the results.</p>
Future Implications discussed	<p>Any type of diet when taught for the purpose of weight loss with enthusiasm and persistence can be effective. Tailoring of diets to suit individual patients on the basis of their personal and cultural preferences may enable more long term success.</p>

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Why was study done? What was perceived general importance?	To evaluate the effects of a high-protein intake on insulin sensitivity and body composition in the context of T2D patients
Is there a clear hypothesis and objectives?	The hypothesis is that a HP diet will improve insulin resistance in T2D after weight loss and reduce fasting and postprandial glucose and insulin concentrations. Also proposed was that the preservation of lean mass in the HP diet leads to an improvement in insulin mediated glucose uptake as compared with the LP diet.
What specific question is being addressed?	Is there an improvement in insulin-mediated glucose uptake and preservation of lean mass with a high-protein diet as compared with a low-protein diet?
The study setting- where did study take place?	The 12 week study was conducted on an outpatient basis and consisted of an 8 week energy restriction component (1600 kcal) followed by a 4 week period of the same macronutrient composition but in energy balance.
Group actually studied	A total of 66 subjects with type 2 diabetes and no proteinuria were recruited by public advertisement. Subjects attended detailed information sessions, and all gave written informed consent. No payment was provided for participation in the study. Of the 54 subjects (19 men, 35 women), 25 managed their diabetes by diet alone, 26 required oral hypoglycemic medications (19 on metformin, 15 sulfonylureas alone or combination), and 4 required insulin. Four subjects with fasting plasma glucose (FPG) of 4–6 mmol/l were asked to cease medications before commencement of the diet to allay possible hypoglycemic episodes with weight loss. Decreases in dosage occurred in eight subjects at weeks 4 and 8 (five from the HP diet and three from the LP diet). Subjects on antihypertensive or lipid-lowering medication were asked to maintain the same dose throughout the study. All subjects were asked to maintain exercise programs at levels established before the study.
The social, cultural, economic, ethnic background	Subjects with T2D recruited by public advertisement.
Study Approval	Study design approved by the Human Ethics Committee of the Commonwealth Scientific and Industrial Research Organisation (CSIRO). All subjects gave written informed consent.
Was there clear inclusion and exclusion criteria and explanations of patient drop out?	Of the subjects, 54 completed the study. Two subjects withdrew before commencement. A further 10 subjects (5 from each diet group) withdrew throughout the study.
Is there a power calculation to determine sample size?	None evident.
Was there selection bias?	None evident

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Was there funding bias?	None evident. Financial contribution from Meadow lea foods.
Confounding Factors	Medications used.
How does the study group relate to researchers interest groups / patients?	Potentially diabetics would be clients of the researcher. The target endpoints of insulin resistance, glucose uptake and preservation of lean tissue and the effects on these by manipulating diet are of relevance to this researcher.
What was the intervention and how was it carried out?	<p>Subjects were matched on the basis of Fasting Plasma Glucose, BMI, age, sex, and medication and were randomly assigned to either the HP diet (30% protein, 40% CHO) or LP diet (15% protein, 60% CHO). The 12-week study was conducted on an outpatient basis and consisted of an 8-week energy restriction component (1,600 kcal) followed by a 4-week period of the same macronutrient composition but in energy balance.</p> <p>Body composition was determined by dual-energy X-ray absorptiometry at weeks 0 and 12.</p> <p>The HP diet consisted of 30% energy from protein and 40% energy from CHO, and the LP diet consisted of 15% energy from protein and 60% energy from CHO. Diets were matched for fatty acid profile (8% saturated fatty acids, 12% monounsaturated fatty acids, 5% polyunsaturated fatty acids).</p> <p>The diets were prescriptive fixed menu plans, and subjects were supplied with key foods, which amounted to 60% of energy intake, to assist with dietary compliance.</p> <p>These included pre-weighed portions of beef and chicken suitable for six meals per week and shortbread biscuits plus low-fat cheese (3% fat), diet yogurt, and skim milk powder for the HP diet and rice for the LP diet. The other differences between the diets lay in the amount of meat and chicken (200 vs. 100 g), fruit (200 vs. 300 g), and whole-meal bread (3 vs. 4 slices). Alcohol was not permitted, and a list of free choice vegetables and salad (maximum 2.5 cups) was provided. During the stable weight phase, caloric intake was increased by 30%, with a further 7 g protein in the LP diet and 21 g in the HP diet.</p>
What was measured and how was it measured?	Subjects attended the clinic for venous blood samples on 2 consecutive days at weeks 0, 4, 8, and 12 after a 12-h fast. Weight was recorded in light clothing at each visit. At weeks 0, 8, and 12, all subjects underwent a 75-g 3-h oral glucose tolerance test (OGTT) with venous blood samples taken fasting and at 1, 2, and 3 h. Subjects collected 24 h urine samples for assessment of urea/ creatinine ratio at weeks 0, 8 and 12.
Were baseline measures used?	Subjects were matched for BMI, age, sex, FPG, and medication. There were no significant differences between two groups for weight or blood pressure.

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Were process measures used?	<p>Each subject completed weighed daily diet checklists of all foods and was assessed by the same dietitian at 2-week intervals. Group training was provided in the use of scales and keeping food records. Three consecutive days (1 weekend and 2 weekdays) of the checklist from each 2-week period were analyzed by Diet/1 Nutrient Calculation software (Xyris Software 1998, Highgate Hill, Australia). This program had no missing values for the nutrients of interest, and because the diet was very prescriptive, unusual foods were rarely encountered. Recipes were entered as proportions of the original ingredients. The database had been extensively modified by our group to add new foods and recipes.</p> <p>Body composition - For assessment of body fat amount and distribution, all subjects underwent a dual-energy X-ray absorptiometry (DEXA; Norland, Fort Atkinson, WI) scan at weeks 0 and 12.</p> <p>Abdominal fat mass was measured from the area demarcated by the ribs at the upper portion and the ileac crests at the lower portion. DEXA calculates the percentage of lean and fat mass based on measured tissue density and the known density of the two tissue types. The CV of these measures was 3– 4%.</p> <p>Insulin sensitivity - At weeks 0 and 12, 25 subjects (8 men, 17 women), not on diabetes medication, underwent a continuous low-dose glucose and insulin infusion test (LDIGIT) for determination of steady-state plasma glucose (SSPG) and steady-state plasma insulin (SSPI) concentrations. The method, a refinement of the modified Harano test previously described (18), involved the insertion of a cannula into a forearm vein for infusion of a combination of insulin and glucose. From a cannula inserted into the opposite forearm, blood samples (under a warmed blanket) were taken at baseline and at 120, 130, 140, 145, and 150 min after commencement of the infusion. SSPG and SSPI concentrations were determined from the average of the samples taken between 120 and 150 min. Subjects were required to lie quietly in a supine position for the duration of the test.</p> <p>Biochemical analysis - Fasting blood samples were collected in tubes containing either no additives for lipids and insulin or sodium fluoride/ EDTA for glucose measurements. Plasma or serum was isolated by centrifugation at 600g for 10 min at 5°C (Beckman GS-6R centrifuge; Beckman, Fullerton, CA) and frozen at -20°C. Biochemical assays were performed in a single assay at the completion of the study, except LDIGIT glucose samples, which were analyzed after each test.</p> <p>Plasma glucose and serum total cholesterol and triacylglycerol concentrations were measured on a Cobas-Bio centrifugal analyzer (Roche, Basel) by using enzymatic kits (Roche) and control sera.</p> <p>Plasma HDL cholesterol concentrations were measured using a Cobas-Bio analyzer after precipitation of LDL and VLDL cholesterol with polyethylene glycol 6000 solution. A modified Friedewald equation was used to calculate LDL cholesterol (19). Insulin was determined in duplicate using a radioimmunoassay kit (Pharmacia & Upjohn Diagnostics, Uppsala, Sweden). HbA1c samples were frozen at -20°C and analyzed by high-performance liquid chromatography at the end of the study. Urine samples to assess compliance to the diet and albumin excretion were frozen, and urea and creatinine were measured in one run on a Hitachi autoanalyzer (Roche, Indianapolis, IN) at the end of the study.</p>
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Were process measures used? – Contd.	Statistical analysis- Analysis was performed by repeated measures ANOVA (with covariates of baseline weight and total fat mass in some analyses) with variables measured at weeks 0, 4, 8, and 12 using SPSS for Windows 10.0 statistical software (SPSS, Chicago). Diet and sex were between-subject factors. One-way ANOVA was used to exclude significant differences at baseline between diets and men and women. Inclusion of data from subjects with medication changes significantly affected the results for the OGTT; therefore, these eight subjects were excluded from analysis in this test. Significance was set at $P < 0.05$.
Were outcome measures identified? Are there clear validated outcomes?	Primary Outcome Measures: Body composition including weight, body fat levels, abdominal fat mass, Insulin sensitivity; Plasma glucose, serum cholesterol and triacylglycerol concentrations, HDL and LDL cholesterol; HbA1c; Compliance to diet and albumin excretion via urine samples ; urea and creatinine
Are the methods quantitative or qualitative?	Both
Safety Results	None reported
Are there end points other than those reported that might be relevant and important	Renal function and bone health maybe relevant due to high-protein arm of study. Apo lipoprotein a and b.
Are the endpoints relevant to actual practice	Yes and consistent with other studies
Dietary Intake and Adherence Results	Energy intake in the 8-week energy restriction phase and the 4-week energy balance phase was not different between the two diets (Table 2). As planned, protein intake was higher and CHO intake lower in the HP diet than in the LP diet both in energy restriction and energy balance ($P < 0.001$), with no differences between phases. Saturated fat intake was not different between the diets or the phases, but dietary fiber and dietary cholesterol were significantly different between diets in both phases.
Weight loss and cardio-protective mechanisms identified,	None highlighted.
Weight Loss / Body Composition results	Overall weight loss of 5.2 ± 1.8 kg achieved independently of diet composition. Women on the HP diet lost significantly more total fat (5.3 vs. 2.8 kg, $P=0.009$) and abdominal fat (1.3 vs. 0.7 kg $P=0.006$) compared with women on the LP diet. In men there was no difference in fat loss between diets 3.9 vs. 5.1kg. Total lean mass decreased in all subjects independent of diet composition. Both men and women lost weight on both diets; however, there was a weak sex by diet interaction ($P=0.04$), such that men lost more weight on the LP diet (5.8 vs. 4.7 kg), whereas women lost more weight on the HP diet (6 vs. 4.2 kg). Similarly for total fat mass, men lost more on the LP diet (5.1 vs. 3.8 kg), whereas women lost more on the HP diet (5.3 vs. 2.8 kg), as reflected by a significant sex by diet interaction ($P=0.01$). A significant sex by diet effect was also observed in the change in abdominal fat mass ($P < 0.02$), such that men lost more fat on the LP diet (1.7 vs. 1.4 kg), whereas women lost more on the HP diet (1.3 vs. 0.7 kg). Total lean mass was reduced significantly with both diets (1.35 kg on the LP diet and 0.52 kg on the HP diet) with no significant difference between them.

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Ketonuria Results	None noted
Cardiac Risk Factor Results	<p>Both dietary patterns resulted in improvements in the CVD risk profile as a consequence of weight loss.</p> <p>Greater reduction in LDL cholesterol in both sexes. LDL cholesterol reduction was significantly greater on the HP diet (5.7%) than on the LP diet (2.7%) ($P < 0.01$).</p> <p>Total cholesterol concentrations decreased more on the HP diet than on the LP diet, as reflected by a diet by time interaction of $P = 0.009$.</p> <p>For all subjects, triacylglycerol concentrations decreased at week 12 ($P < 0.001$), and there was no diet or sex effect. There was no effect of time or diet for HDL cholesterol concentrations.</p> <p>Blood pressure - Systolic blood pressure fell significantly by 8 mmHg and diastolic blood pressure by 4 mmHg at week 8 ($P < 0.001$) with no differential effect of diet. During the weight stabilization period between weeks 8 and 12, systolic blood pressure rose by 3 mmHg and diastolic blood pressure by 1 mmHg ($P < 0.001$). This was also not affected by diet composition.</p>
Hormonal and Endocrine Results	<p>Glycemic control</p> <p>Fasting and 1-, 2-, and 3-h plasma glucose concentrations were reduced by both dietary interventions ($P < 0.001$); however, no significant effects of diet or sex were observed.</p> <p>Fasting and 2-h insulin concentrations were reduced at weeks 8 and 12 (both $P < 0.001$). The insulin:glucose product was reduced by 42% at 3 h at week 12. HbA1c decreased by 9.4% between baseline and week 12 ($P < 0.001$). There were no significant differences observed for diet or sex.</p>
Exercise and Medication use	Subjects asked to maintain exercise programmes at levels established before the study.
What effect may bias have on the result?	None evident.
The Author's conclusions - are these justified?	<p>HP is a valid diet choice for reducing CVD risk in T2D.</p> <p>Both dietary patterns resulted in improvements in the cardiovascular disease (CVD) risk profile as a consequence of weight loss. However, the greater reductions in total and abdominal fat mass in women and greater LDL cholesterol reduction observed in both sexes on the HP diet suggest that it is a valid diet choice for reducing CVD risk in type 2 diabetes.</p> <p>In this study, both HP and LP diets decreased weight, fasting glucose, and insulin concentrations as well as total and abdominal fat. However, in women, the HP diet was able to decrease total and abdominal fat differentially compared with the LP diet.</p>

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The Author's conclusions - are these justified? contd.	<p>In addition, the HP diet significantly decreased LDL cholesterol concentrations in both men and women compared with the LP diet.</p> <p>In our study, subjects lost an absolute 2.1% lean mass overall with no significant difference between the two diets.</p>
Generalizability- the extent to which the results might apply outside the study	Weight loss and CVD marker improvement with energy restriction may be generalized. The specific sex-specific effect of the HP diet on total and abdominal fat in women but not men needs to be explored further.
Discussion points	<p>Steady state plasma glucose (SSPG) concentrations were significantly decreased at week 12, indicating that subjects became more insulin sensitive. SSPI concentrations were also significantly reduced at week 12, but this may reflect the decrease in infused insulin (due to a lower body weight) or an enhanced clearance and not necessarily a decrease in insulin secretion.</p> <p>Greater energy restriction, (800 vs. 1,600 kcal), higher protein levels, and the inclusion of only glucose-tolerant women may have affected the disparity in outcomes between the study of Piatti et al. (13), who found that HP weight loss diets spared lean body mass, and our study. This study used DEXA for estimating body composition in obese subjects with type 2 diabetes, whereas Piatti et al. (13) used anthropometry. DEXA is a more accurate method of determination of body fat distribution when compared with traditional anthropometric methods, such as skinfold thickness measurements and waist-to-hip ratio.</p> <p>Despite greater fat loss, the women on the HP diet were apparently not more insulin sensitive than the men or women who lost less fat. A possible explanation for this may be the small differential fat loss (2.5 kg), which may not have been large enough to produce a significant change in insulin sensitivity, as assessed by the low-dose glucose and insulin infusion test (LDIGIT) or the oral glucose tolerance test (OGTT). Longer-term studies with greater weight loss might reveal such differences.</p> <p>Both diets were low in saturated fat and cholesterol. In contrast to the findings of this study, Wolfe and Giovanetti (23) found significant decreases in triglyceride concentrations as well as increases in HDL cholesterol concentrations on the HP diet. Although triglyceride concentrations were improved, in this study, there was no difference between the diets.</p> <p>This study found a significant decrease in LDL cholesterol at all time points from baseline in both men and women on the HP diet compared with the LP diet. There was no impact of body composition changes on this result. Because saturated fat intake was not different between the diets, this was not the cause of the differential LDL cholesterol reduction. The mechanism for the hypolipidemic effect of an HP intake on LDL cholesterol concentrations is unclear.</p>
Were study limitations discussed?	C-Peptide concentrations were not measured which could indicate whether endogenous insulin secretion had reduced.

APPENDIX A10: Data Collection Sheets- Parker et al. 2002

(Some sections of text and/or data extracted verbatim from the reference paper. Figure, Table and Numerical references included in brackets refer to the original article).

Future Implications discussed	<p>The novel observation of a possible sex-specific effect of the HP diet on total and abdominal fat loss in women but not men requires confirmation. Although this result may reflect the small number of male subjects in both dietary interventions, there was no suggestion that the HP diet was advantageous in men.</p> <p>The observed decrease in LDL cholesterol concentrations of 5.7% on the HP diet may lead to a 10% decrease in the risk of CVD in these subjects. This result is relevant because in people with type 2 diabetes, the risk of CVD is increased two to four times that of the normal population (1). However, because this effect on LDL has not been observed before with HP weight loss diets, further confirmatory work is required.</p>
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APPENDIX A11: Data Collection Sheets – Sacks et al. (2009)

(Text and/or data extracted verbatim from study article for many of the descriptive sections. Figure, Table and Numerical references included in brackets refer to the original article).

Author	Sacks et al. (2009)
Title	Comparison of Weight-Loss Diets with Different Compositions of Fat, Protein, and Carbohydrates
Journal	The New England Journal of Medicine
Quality of Journal and competence of Researchers	Peer Reviewed Journal. 17 Authors listed – 5 of whom are MDs and 6 are PhDs. FM Sacks is a member of the Department of Nutrition. Harvard School of Public Health
General Aim Clear	To assess the significance of the macronutrients on weight loss over one year. The crucial question is whether overweight people have a better response in the long term to diets that emphasize a specific macronutrient composition.
Specific Study objectives stated	To compare the effects of three principal dietary macronutrients over two years, recognizing that weight loss typically is greatest 6-12 months after initiation of the diet with steady regain of weight subsequently.
Aim and study objectives relevant to research question being explored External Validity - relevance of this particular piece of work to the issue under scrutiny	Relevant to primary research question as to whether the macronutrient composition of a diet is significant to weight management and cardiovascular disease (CVD) risk management. Two lower-carbohydrate diet plans where carbohydrate was 35% and 45 % of energy similar to the Zone type diet compared with 2 diets with a low-fat/higher carbohydrate design.
Internal Validity - methods and actual results in the light of study objectives	Randomized , comparative intervention
Study described as randomised	Yes 811 overweight adults randomly assigned to one of 4 diets. The targeted percentages of energy from fat, protein and carbohydrates (CHO) in the four diets.
Study described as double blind	No
Description of withdrawals and dropouts present	Of 1638 participants who were screened, 811 (50%) were randomly assigned to a diet, and 645 (80% of those assigned) completed the study (i.e., provided a body-weight measurement at 2 years) Detailed description of dropouts and participants are available in the supplementary index. Of 201 allocated to HF/HP (40%F:25%P:35%Carb), 168 completed; 6 withdrew, 27 lost to follow up of which 19 did not respond to repeated contact, 2 missed scheduled appointment, 1 moved away.

APPENDIX A11: Data Collection Sheets – Sacks et al. (2009)

(Text and/or data extracted verbatim from study article for many of the descriptive sections. Figure, Table and Numerical references included in brackets refer to the original article).

Description of withdrawals and dropouts present contd.	<p>Of 204 allocated to HF/AP (40% Fat, 15% Protein, 45% Carb), 151 completed, 12 withdrew, 41 lost to follow up.</p> <p>Of 202 allocated to LF/HP (20%F:25%P:55% C), 157 completed, 11 withdrew and 34 lost to follow up</p> <p>Of 204 allocated to LF/AP (20%Fat:15%P:65%C) 169 completed, 7 withdrew and 28 were lost to follow up of which 2 moved away, 20 did not respond and 6 did not meet scheduled appointment.</p>
Randomisation / blinding appropriate	<p>Blinding was maintained by use of similar foods for each diet.</p> <p>Staff and participants were advised that each diet adhered to principles of a healthful diet and recommended for long term weight loss thereby establishing equipoise. Staff who measured outcomes were unaware of the diet assignment of the participants.</p>
Target Population	Overweight and obese 30-70 year old Adult Subjects
Why was study done? What was perceived general importance?	<p>To conduct a large trial designed to overcome limitations of previous trials comparing the effects of the three macronutrients. Limitations noted were small samples, underrepresentation of men, limited generalizability, a lack of blinded ascertainment of the outcome, a lack of data on adherence to assigned diets and a large loss to follow up.</p> <p>Weight loss studied over course of 2 years to evaluate the weight loss, weight regain and plateaux phases.</p>
Is there a clear hypothesis and objectives?	Not clearly stated but implied hypothesis relates to the importance of macronutrient levels for weight management.
What specific question is being addressed?	Whether macronutrient composition affects weight management.
The study setting- where did study take place?	Trial conducted at 2 sites: The Harvard School of Public Health and Brigham and Women's Hospital Boston; and the Pennington Biomedical Research Centre of the Louisiana State University
Group actually studied	Overweight and obese generally healthy adults ensuring the inclusion of adequate number of male subjects
The social, cultural, economic, ethnic background	Overweight and obese subjects of which 40% would be men.
Study Approval	The study was approved by the National Heart Lung and Blood Institute.
Was there clear inclusion and exclusion criteria and explanations of patient drop out?	<p>Inclusion criteria: Participants had to be 30-70 years of age and have a body mass index of 25-40.</p> <p>Exclusion Criteria: presence of Diabetes treated with oral medications or insulin or unstable CVD; use of medication that affects body weight and insufficient motivation as assessed by interview and questionnaire.</p>

APPENDIX A11: Data Collection Sheets – Sacks et al. (2009)

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Is there a power calculation to determine sample size?	The study was powered to detect a 1.67-kg weight loss as an effect of the level of protein or fat in the diet over the 2-year period, assuming a withdrawal rate of 40%.
Was there selection bias?	Not evident.
Was there funding bias?	None evident. The study was supported by grants from the National, Heart, Lung and Blood Institute.
Confounding Factors	None noted.
How does the study group relate to researchers interest groups / patients?	The researcher's interest groups would potentially include overweight and/or obese adults
What was the intervention and how was it carried out?	<p>The nutrient goals for the 4 diet groups. 20% fat, 15% protein and 65% carbohydrates (CHO) the low-fat average-protein plan(LFAP); 20% fat, 25% protein and 55% CHO the low fat, high protein plan (LFHP); 40% fat, 15% protein and 45% CHO- the high fat, average protein plan (HFAP); and the 40% fat, 25% protein and 35% CHO- the high fat, high-protein plan (HFHP).</p> <p>Design: 2 by 2 factorial design and allowed a dose response test of CHO intake that ranged from 35 to 65% of energy.</p> <p>Other goals for all groups were that diets should include 8% or less of saturated fat, at least 20g of dietary fibre and 150mg or less of cholesterol per 1000kcal. Carbohydrate rich foods with a low glycemic index were recommended in each diet.</p> <p>Each person had a caloric prescription of a 750 kcal deficit per day from baseline as calculated from the participant's resting energy expenditure and activity level. No initial diet had less than 1200kcal/d.</p> <p>Group sessions were held once a week, 3 of every 4 weeks during the first six months and 2 of every 4 weeks from 6 months to 2 years. Individual sessions were held every 8 weeks for entire two years.</p> <p>Daily meal plans in 2-week blocks were provided.</p> <p>Participants were instructed to record their food and beverage intake in a daily food diary in a web based self-monitoring tool. Behavioural counselling was integrated to promote adherence to the assigned diets.</p> <p>Contact among the groups was avoided.</p> <p>The goal for physical activity was 90 minutes per week.</p> <p>Participation in exercise was monitored by questionnaire and by an online self-monitoring tool.</p>

APPENDIX A11: Data Collection Sheets – Sacks et al. (2009)

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What was measured and how was it measured?	<p>Body weight and waist circumference were measured in the morning before breakfast on 2 days at baseline, 6 months, and 2 years, and on a single day at 12 and 18 months.</p> <p>Dietary intake was assessed in a random sample of 50% of the participants, by a review of the 5-day diet record at baseline and by 24-hour recall during a telephone interview on 3 non-consecutive days at 6 months and at 2 years.</p> <p>Questionnaires that asked for information on satiety, food craving, eating behaviour, and satisfaction with the diet were administered at baseline (except for diet satisfaction) and at 6 months and 2 years.</p> <p>Fasting blood samples, 24-hour urine samples, and measurement of resting metabolic rate were obtained on 1 day, and blood-pressure measurement on 2 days, at baseline, 6 months, and 2 years.</p> <p>Levels of serum lipids, glucose, insulin, and glycated haemoglobin were measured at the clinical laboratory at the Pennington Biomedical Research Centre.</p> <p>Blood pressure was measured with the use of an automated device (HEM-907XL, Omron). The participants were evaluated for the presence of the metabolic syndrome, which was defined by the presence of at least three of the following five criteria: waist circumference of more than 102 cm in men or more than 88 cm in women, a triglyceride level of 150 mg per deciliter (1.69 mmol per litre) or more, a high density lipoprotein (HDL) cholesterol level of less than 40 mg per deciliter (1.03 mmol per litre) in men or less than 50 mg per deciliter (1.29 mmol per litre) in women, a blood pressure of 130/85 mm Hg or more, and a fasting glucose level of 110 mg per deciliter (6.1 mmol per litre) or more.</p>
Were baseline measures used?	Baseline characteristics were similar among participants assigned to the four diets and between those who were assigned to a diet and those who completed the study.
Were process measures used?	<p>Statistical Analysis</p> <p>Data were pooled from the diets for the two factorial comparisons: low fat versus high fat and average protein versus high protein. The analysis also included a comparison of two of the four diets, the diet with the lowest carbohydrate content and the diet with the highest carbohydrate content, and included a test for trend across the four levels of carbohydrates.</p> <p>The effects of protein, fat, and carbohydrate levels were evaluated independently with the use of two-sample t-tests at a two-sided significance level of 0.05.</p> <p>Exploratory post hoc analyses were performed with threshold amounts of weight loss as outcomes, with Bonferroni's adjustment for multiple comparisons.</p> <p>Associations between adherence to the fat and protein goals and weight loss were also explored in post hoc analyses.</p> <p>An intention-to-treat analysis was performed in which long-term weight loss for persons who withdrew from the study early (after at</p>

APPENDIX A11: Data Collection Sheets – Sacks et al. (2009)

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Were process measures used? contd.	<p>least 6 months of participation) was imputed on the basis of a rate of 0.3 kg per month of regained weight and a rate of 0.3 cm per month of regained waist circumference after withdrawal.</p> <p>Risk factors for cardiovascular disease and diabetes were also analyzed according to the intention-to-treat principle, with zero change from baseline imputed for missing data.</p>
Were outcome measures identified? Are there clear validated outcomes?	Yes
Are the methods quantitative or qualitative?	Both quantitative and qualitative
Safety Results	<p>Adverse events were reported by 57 participants (7%); there were no significant differences in the rates among diets.</p> <p>The ratio of urinary microalbumin to creatinine was more than 30 in five participants in the average-protein group and in five participants in the high-protein group at 6 months and in seven participants, all in the average protein groups, at 2 years.</p> <p>There was a larger decrease in urinary nitrogen excretion from baseline in the average-protein group than in the high protein group (a difference in the change of 1.6 g at 6 months and 0.8 g at 2 years. These differences correspond to a difference in dietary protein of 10 g per day and 5 g per day, respectively.</p>
Endpoint/ Biomarker Tested	The primary outcome of the study was the change in body weight over a period of 2 years, and the secondary outcome was the change in waist circumference
Are there end points other than those reported that might be relevant and important	Apo lipoprotein a and b
Are the endpoints relevant to actual practice	Yes
Dietary Intake and Adherence Results	<p>Mean reported intakes at 6 months and 2 years did not reach the target levels for macronutrients. The reported intakes represented differences from target levels of fat, protein, and carbohydrate intake of 8.0, 4.2, and 14.4 percentage points, respectively, at 6 months and 6.7, 1.4, and 10.2 percentage points, respectively, at 2 years.</p> <p>Reported energy intakes and physical activity were similar among the diet groups.</p> <p>The participants who completed the study had a mean weight loss of 6.5 kg at 6 months, which corresponds to a reduction in daily energy intake of approximately 225 kcal.</p> <p>The respiratory quotient was 0.84 at baseline in both the high-fat and low-fat groups, and the between-group difference in the</p>

APPENDIX A11: Data Collection Sheets – Sacks et al. (2009)

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<p>Dietary Intake and Adherence Results contd.</p>	<p>change at 2 years (the value in the high-fat group minus the value in the low-fat group) was -0.02 ($P = 0.002$).</p> <p>Thus, changes in biomarkers confirmed that differences among the groups in macronutrient intake were consistent with those recorded in the dietary reports and that participants modified their intake of macronutrients in the direction of the goals, although the targets were not fully achieved.</p> <p>Adherence to the goal for protein intake was associated with more weight loss only in the high protein groups, and adherence to the goal for fat intake was associated with more weight loss only in the low-fat groups ($P < 0.001$).</p>
<p>Weight loss and cardio-protective and other mechanisms identified,</p>	<p>Craving, fullness, and hunger and diet-satisfaction scores were similar at 6 months and at 2 years among the diets.</p> <p>Attendance at group sessions strongly predicted weight loss at 2 years (0.2 kg for every session attended) and was similar among the diet groups</p>
<p>Weight Loss / Body Composition results</p>	<p>Weight Loss At 6 months, participants assigned to each diet had lost an average of 6 kg, which represented 7% of their initial weight; they began to regain weight after 12 months.</p> <p>By 2 years, weight loss remained similar in those who were assigned to a diet with 15% protein and those assigned to a diet with 25% protein (3.0 and 3.6 kg, respectively); in those assigned to a diet with 20% fat and those assigned to a diet with 40% fat (3.3 kg for both groups); and in those assigned to a diet with 65% carbohydrates and those assigned to a diet with 35% carbohydrates (2.9 and 3.4 kg, respectively) ($P > 0.20$ for all comparisons). Among the 80% of participants who completed the trial, the average weight loss was 4 kg; 14 to 15% of the participants had a reduction of at least 10% of their initial body weight.</p> <p>Satiety, hunger, satisfaction with the diet, and attendance at group sessions were similar for all diets; attendance was strongly associated with weight loss (0.2 kg per session attended).</p> <p>The change in waist circumference did not differ significantly among the diet groups.</p> <p>Most of the weight loss occurred in the first 6 months. Changes from baseline differed among the diet groups by less than 0.5 kg of body weight and 0.5 cm of waist circumference.</p> <p>After 12 months, all groups, on average, slowly regained body weight. A total of 185 of the participants (23%) continued to lose weight from 6 months to 2 years. The mean (\pmSD) additional weight loss was 3.6 ± 3.5 kg, for a mean total loss from baseline of 9.3 ± 8.2 kg, with no significant differences among the diet groups.</p> <p>At 2 years, 31 to 37% of the participants had lost at least 5% of their initial body weight, 14 to 15% of the participants in each diet</p>

APPENDIX A11: Data Collection Sheets – Sacks et al. (2009)

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Weight Loss / Body Composition results – Contd.	group had lost at least 10% of their initial weight, and 2 to 4% had lost 20 kg or more (P>0.20 for the comparisons between diets).
Cardiac Risk Factor Results	<p>All the diets reduced risk factors for cardiovascular disease and diabetes at 6 months and 2 years.</p> <p>At 2 years, the two low-fat diets and the highest-carbohydrate diet decreased low-density lipoprotein cholesterol levels more than did the high-fat diets or the lowest-carbohydrate diet (low-fat vs. high-fat, 5% vs. 1% [P = 0.001]; highest carbohydrate vs. lowest-carbohydrate, 6% vs. 1% [P = 0.01]).</p> <p>The lowest-carbohydrate diet increased HDL cholesterol levels more than the highest-carbohydrate diet (9% vs. 6%, P = 0.02). There was a larger increase from baseline in the HDL cholesterol level, a biomarker for dietary carbohydrate, in the lowest-carbohydrate group than in the highest-carbohydrate group (a difference in the change of 2 mg per deciliter at 2 years). This difference corresponds to a predicted difference in carbohydrate intake of 6%.</p> <p>All the diets decreased triglyceride levels similarly, by 12 to 17%.</p> <p>Blood pressure decreased from baseline by 1 to 2 mm Hg, with no significant differences among the groups (P>0.59 for all comparisons).</p> <p>These changes in risk factors in the intention-to-treat population were about 30 to 40% smaller than the changes seen among participants who provided data at 2 years, reflecting the effect of the imputation of missing values</p>
Endocrine markers and Hormonal Effects	<p>All the diets except the one with the highest carbohydrate content decreased fasting serum insulin levels by 6 to 12%; the decrease was larger with the high-protein diet than with the average-protein diet (10% vs. 4%, P = 0.07).</p> <p>The metabolic syndrome was present in 32% of the participants at baseline, and the percentage was lower at 2 years, ranging from 19 to 22% in the four diet groups (P = 0.81 for the four-way comparison).</p>
Exercise and Medication use	<p>Physical Activity goals were established for sedentary participants gradually increasing from 30 minutes of moderate intensity per week to 90 minutes per week during first 6 months Participants were encouraged to do more if they could. Minutes of exercise were monitored using self-monitoring forms.</p> <p>Reported physical activity was similar among the diet groups.</p>
What effect may bias have on the result?	None evident

APPENDIX A11: Data Collection Sheets – Sacks et al. (2009)

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The Author's conclusions - are these justified?	Diets that are successful in causing weight loss can emphasize a range of fat, protein, and carbohydrate compositions that have beneficial effects on risk factors for cardiovascular disease and diabetes. Such diets can also be tailored to individual patients on the basis of their personal and cultural preferences and may therefore have the best chance for long-term success.
Generalizability- the extent to which the results might apply outside the study	The four different dietary strategies representing differing percentages of various macronutrients provide clinical options to consider when making dietary recommendations.
Discussion points	<p>The principal finding is that the diets were equally successful in promoting clinically meaningful weight loss and the maintenance of weight loss over the course of 2 years.</p> <p>Satiety, hunger, satisfaction with the diet, and attendance at group sessions were similar for all diets.</p> <p>The diets improved lipid risk factors and fasting insulin levels in the directions that would be expected on the basis of macronutrient content.</p> <p>The study had a large sample, a high rate of retention, and the sensitivity to detect small changes in weight.</p> <p>The findings should be directly applicable to both clinicians' recommendations for weight loss in individual patients and the development of population-wide recommendations by public health officials.</p> <p>Despite the intensive behavioural counselling in the study, participants had difficulty achieving the goals for macronutrient intake of their assigned group. The mean differences among the groups in fat, carbohydrate, or protein intake at 6 months were nevertheless often greater than those in several previous trials comparing diets for weight loss.</p> <p>Substantially diminished adherence after the first few months is typical in weight loss trials and occurred between 6 months and 2 years in our trial.</p> <p>Only two trials have reported dietary intake beyond 1 year and one of them provided foods to the participants.</p> <p>In addition, trials of low-carbohydrate diets have reported a very low incidence of urinary ketosis after 6 months suggesting that in most overweight people, it is futile to sustain a low intake of carbohydrates.</p> <p>Overall, these findings with respect to adherence to macronutrient goals suggest that participants in weight-loss programs revert to their customary macronutrient intakes over time but may nonetheless be able to maintain weight loss.</p> <p>Attendance had a strong association with weight loss, and the association was similar across diet groups. The Authors view attendance at counselling sessions as a proxy for commitment to achieving weight loss.</p>

APPENDIX A11: Data Collection Sheets – Sacks et al. (2009)

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Discussion points – contd.	<p>Study participants who attended two thirds of the sessions over the course of 2 years lost about 9 kg of weight.</p> <p>Regain after 6 to 12 months was about 20% of the regain reported in earlier trials. Several recent trials have also shown that continued contact with participants after weight loss is associated with less regain. These findings together point to behavioural factors rather than macronutrient metabolism as the main influences on weight loss.</p> <p>The authors used a generic approach to developing each diet and the instructions for following it, in order to minimize Influences media attention, cultural norms or scientific novelty.</p> <p>No diet was considered to be a control diet, and the dietary counselling and the attention that we provided were the same for all diet groups throughout the study period.</p> <p>The authors did not confirm previous findings that low-carbohydrate or high protein diets caused increased weight loss at 6 months and that the advantage of these diets usually eroded by 12 months, with weight loss that was nearly or fully equivalent to that with low-fat diets.</p> <p>Other studies showed increased weight loss at 1 to 2 years with diets that were high in unsaturated fat or with low-fat, high-carbohydrate vegetarian diets.</p> <p>When non nutritional influences are minimized, as they were in this study, the specific macronutrient content is of minor importance as was suggested many years ago.</p>
Were study limitations discussed?	Association of achieved nutrition with weight loss explored. These post hoc analyses do not have the strong validity of the main analysis which compared randomized groups. Protein and fat intakes overlapped hence confounding the results.
Future Implications discussed	Any type of diet when taught for the purpose of weight loss with enthusiasm and persistence can be effective. Tailoring of diets to suit individual patients on the basis of their personal and cultural preferences may enable more long term success.

APPENDIX A 12: Data Collection Sheets – Samaha et al. (2003)

(Some text and/or data extracted verbatim from study article for many of the descriptive sections. Figure, Table and Numerical references included in brackets refer to the original article).

Author	Samaha et al. (2003)
Title	A Low-Carbohydrate as Compared with a Low-Fat Diet in Severe Obesity
Journal	The New England Journal of Medicine
Quality of Journal and competence of Researchers	Peer Reviewed Journal. 4 out of 10 authors are MDs.
General Aim Clear	To assess how restricting carbohydrates affects weight loss and serum lipid concentrations.
Specific Study objectives stated	To test the hypothesis that severely obese subjects with diabetes or metabolic syndrome would have greater weight loss without detrimental effects on risk factors for atherosclerosis while on a carbohydrate (CHO) reduced diet than on a calorie and fat restricted low- fat diet.
Aim and study objectives relevant to research question being explored External Validity - relevance of this particular piece of work to the issue under scrutiny	Relevant to primary research question as to whether the macronutrient composition of a diet and particularly CHO restriction is significant to weight management and CVD risk management. Low-Carbohydrate Atkins type diet compared to a low-fat conventional diet over 6 months.
Internal Validity - methods and actual results in the light of study objectives	Randomized comparative intervention.
Study described as randomised	Random assignation of subjects to one of two diets
Study described as double blind	No
Description of withdrawals and dropouts present	Between May 2001 and November 2001, 132 persons were randomly assigned to either a low-carbohydrate diet ($n=64$) or a conventional diet ($n=68$). By six months 79 subjects remained – 36 in the LF group and 43 in the low CHO group. The primary analysis included all 132 subjects – 79 who completed study; 29 who dropped out but had six-month data from routine visits and 24 for whom weight recorded at the last follow up was carried forward. A second analysis included all subjects for all 53 subjects who dropped out.
Randomisation / blinding appropriate	Randomisation appropriate ; Blinding not relevant
Target Population	Severely obese Adults

APPENDIX A 12: Data Collection Sheets – Samaha et al. (2003)

(Some text and/or data extracted verbatim from study article for many of the descriptive sections. Figure, Table and Numerical references included in brackets refer to the original article).

Why was study done? What was perceived general importance?	The Authors felt that the effects of a carbohydrate-restricted diet on weight loss and risk factors for atherosclerosis have been incompletely assessed
Is there a clear hypothesis and objectives?	Yes. That severely obese subjects with a high prevalence of diabetes or the metabolic syndrome would have greater weight loss without detrimental effects on risk factors for atherosclerosis while on a carbohydrate-restricted diet than on a calorie and fat-restricted low-fat diet.
What specific question is being addressed?	For severely obese individuals, do low-carbohydrate diets work better than conventional low-fat, low-calorie diets?
The study setting- where did study take place?	The Philadelphia Veterans Medical Centre. Department of Medicine – Division of Cardiology.
The study population - Intended group to whom results should apply vs. group actually studied	Severely obese individuals with metabolic disease
Group actually studied	132 subjects were randomly assigned to either low-carbohydrate or low fat diet using random numbers.
The social, cultural, economic, ethnic background	Veterans. A high proportion of black subjects.
Study Approval	Study approved by review board at the Philadelphia Veterans Affairs Medical Centre.
Was there clear inclusion and exclusion criteria and explanations of patient drop out?	Yes. Inclusion criteria of age at least 18 years and BMI of at least 35. Exclusion criteria : serum creatinine level of >1.5mg per decilitre; hepatic disease, life-limiting medical illness; inability of diabetic subjects to monitor own glucose; active participation in a dietary programme or use of weight loss medications
Is there a power calculation to determine sample size?	Assuming a two-sided type 1 error of 5% the authors estimated a need for 100 subjects for the study to have 80% power to demonstrate a mean \pm SD weight loss that was 5 ± 12 v kg greater in the low CHO group than the low fat group. A dropout rate of 25 was anticipated so the enrolment target was 135.
Was there selection bias?	None evident.
Was there funding bias?	None evident.
Confounding Factors	Many of the subjects were taking lipid lowering medication and hypoglycaemic agents.

APPENDIX A 12: Data Collection Sheets – Samaha et al. (2003)

(Some text and/or data extracted verbatim from study article for many of the descriptive sections. Figure, Table and Numerical references included in brackets refer to the original article).

How does the study group relate to researchers interest groups / patients?	Obese and severely obese subjects with evidence of metabolic disease fall in the scope of the researchers interests.
What was the intervention and how was it carried out?	<p>2 diet groups attended separate 2 hour group teaching for 4 weeks followed by one hour sessions for 5 additional months. Subjects received a diet overview handout, instructional nutrition labels, sample menus and recipes and a book on counting calories and carbohydrates. No specific exercise was recommended.</p> <p>Subjects on Low CHO instructed to restrict CHO intake to 30g per day or less. No restriction on total fat intake. Vegetables and fruits with a high ratio of fibre to CHO recommended.</p> <p>Subjects on low-fat diet were recommended the guidelines of the National, Heart, Lung and Blood Institute including caloric restriction sufficient to create a deficit of 500 calories with 30% or less of total calories derived from fat.</p>
What was measured and how was it, measured?	<p>Weight measured monthly on a single calibrated scale; Other data at enrolment and at six months collected included waist size, self reported medical history, blood pressure, glucose and serum lipid levels measured in blood samples obtained after an overnight fast.</p> <p>LDL cholesterol calculated according to the Friedwald formula.</p> <p>Serum insulin measured by radioimmunoassay; Insulin sensitivity estimated with use of the quantitative insulin –sensitivity check index.</p> <p>Dietary compliance estimated by a previously validated instrument to obtain a 24hr recall of dietary consumption. Data analysed with Nutribase Management software (Cybersoft)</p>
Were baseline measures used?	Baseline characteristics shown in Table 1 in the paper.
Were process measures used?	<p>For comparison of continuous variables between the two groups, the change from baseline to six months in each subject was calculated and mean changes were compared using an unpaired t test. Normality of the distribution was assessed before using the t-test.</p> <p>Triglyceride, insulin and glucose levels were skewed and were log-transformed for analysis.</p> <p>Dichotomous variables by chi-square analysis.</p> <p>Linear regression and two way analysis of covariance models were used to correct for potentially confounding variables and to identify interactions between variables and diet group assignment.</p>

APPENDIX A 12: Data Collection Sheets – Samaha et al. (2003)

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Were process measures used? Contd.	Missing waist sizes were imputed by linear extrapolation on the basis of height and weight. P values were two-sided and a P value of 0.05 indicated statistical significance SPSS version 10 software used for statistical analysis.
Were outcome measures identified? Are there clear validated outcomes?	Primary end point was weight loss at six months. For analyses of changes in dietary intake, serum lipid levels, glycemic control and insulin sensitivity – all subjects were included with baseline values carried forward for subjects who dropped out of the study.
Are the methods quantitative or qualitative?	Quantitative and qualitative.
Safety Results	No clinically significant change in uric acid levels in either group. One death and hospitalisation in the low CHO group not deemed to be diet related.
Endpoint/ Biomarker Tested	Weight loss, serum lipids, glycemic control and insulin sensitivity, BP, adverse reactions, attrition, assessment of dietary intake.
Are there end points other than those reported that might be relevant and important	Apolipoprotein a and b, renal and bone health as one arm was a ketogenic diet.
Are the endpoints relevant to actual practice	Yes and consistent with other studies.
Dietary Intake and Adherence Results	After 6 months, subjects on the low-fat diet reported a decrease in caloric consumption while the macronutrient composition was close to the guidelines on the NHLBI. Subjects on the low-carbohydrate diet reported a non-significantly greater reduction in caloric intake (P=0.33), a significantly greater decrease in % of calories from CHO (P<0.001) and a significantly greater increase in calories from protein (P<0.001) and fat (P=0.004). ADHERENCE: Cumulative % of drop-outs by months 1, 3 & 6 were 38, 44, and 47 in the low fat group and 25, 27 and 33 % in the low CHO group. Differences in attrition was statistically significant by the 3 rd month (P=0.03) but not at six months (P=0.10). No significant differences between the groups in the characteristics of the subjects who dropped out Subjects in the low-carbohydrate group attended more dietary counselling sessions than the low fat group.

APPENDIX A 12: Data Collection Sheets – Samaha et al. (2003)

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Weight loss and cardio-protective mechanisms identified	<p>Greater weight loss in the low-carbohydrate group suggests a greater reduction in overall caloric intake rather than a direct effect of macronutrient composition. The explanation for this difference is not clear – potentially higher satiety on a diet with liberal portions of protein and fat; simplicity of the diet; improved compliance related to the novelty of the diet.</p> <p>Amount of weight loss had a significant effect on the degree of improvement in metabolic factors including insulin resistance and triglyceride levels. Subjects who lost more than 5% of their baseline weight on a carbohydrate-restricted diet had greater decreases in triglyceride levels than those who lost a similar amount of weight while following a calorie and fat restricted diet.</p> <p>Other uncontrolled variables such as types of carbohydrates selected e.g. proportion of complex carbohydrates or ratio of carbohydrate to fibre may have contributed to effects on improved insulin sensitivity and triglycerides.</p>
Weight Loss / Body Composition results	<p>Subjects on the low CHO diet lost more weight during the six month study than those on the low-fat diet – mean -5.8 ± 8.6 kg vs. -1.9 ± 4.2 kg.</p> <p>95% Confidence Interval for the difference in weight loss between groups -1.6 to -6.3 ($P=0.002$). The difference remained significant after adjustment for baseline variables and for baseline variables plus the number of counselling sessions.</p> <p>The second analysis for dropouts also showed greater weight loss in the low-carb group than in the LF group: -5.7 ± 8.6 kg vs. 1.8 ± 3.9 kg.</p> <p>Weight loss of at least 10% of baseline occurred in 9 of 64 subjects (14%) as compared with 2 of 68 subjects on the low fat diet (3%). White subjects lost more weight than black subjects (mean -13 ± 19 kg vs. -5 ± 12 kg ($P=0.009$)).</p>
Ketonuria Results	None reported.
Cardiac Risk Factor Results	<p>Greater decrease in the mean triglyceride level in the low CHO group than in the low fat group (-20 ± 31 %, $P=0.001$).</p> <p>LCHO subjects had a greater decrease in triglyceride levels irrespective of whether they were on lipid lowering drugs (-25 ± 38 % vs. 8 ± 35 % with lipid lowering drugs – $P=0.01$) and -16 ± 46 % vs. -1 ± 25 % without lipid lowering drugs.</p> <p>In a separate analysis of subjects who were not taking medications – 28 on the low fat diet and 24 on the low CHO diet, the mean reduction in the triglyceride level was greater in the low CHO group : -20 ± 42 % vs. 2 ± 28 %- $P=0.001$)</p> <p>Assignment to the low CHO diet ($P=0.01$) and the amount of weight lost ($P<0.001$) were each independent predictors of a decrease in the triglyceride level however this was limited to subjects who lost more than 5% of base-line weight.</p>

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Cardiac Risk Factor Results contd.	<p>Total cholesterol, HDL and LDL did not change significantly during the six months or between groups.</p> <p>BP: Systolic and diastolic BP decreased by 2mm Hg and 1mm Hg respectively in the low CHO group. In the low fat group both measures decreased by 2mm Hg but there was no significant difference between the groups.</p>
Hormonal & Endocrine Results	<p>Glycemic control: Fasting glucose decreased more in the Low CHO group than the low fat group at six month agents or s $-9\pm 19\%$ vs. $-2\pm 17\%$ ($P=0.02$) though this change was more significant for diabetic subjects with no significant change in the levels in nondiabetic subjects on either diet. Similarly diabetic subjects showed a greater decrease in glycosylated haemoglobin compared with those on low-fat diets.</p> <p>By six months seven subjects in the low CHO group had dose reductions in oral hypoglycaemic or insulin as compared to 1 in the low- fat group.</p> <p>Insulin sensitivity increased more in the low CHO subjects than on the low fat diet. Here again assignment to low CHO diet and weight loss were independent predictors of an improvement in insulin sensitivity.</p>
Exercise and Medication use	Many subjects were taking lipid-lowering medications and hypoglycaemic agents. No comment on exercise.
What effect may bias have on the result?	None noted.
The Author's conclusions - are these justified?	<p>Severely obese subjects with higher prevalence of diabetes and metabolic syndrome lost more weight during six months on a CHO restricted diet than on a calorie and fat restricted diet.</p> <p>Results must be interpreted with caution as magnitude of weight loss in relation to subjects' obesity levels was small.</p> <p>Unclear if the benefits of a low CHO extend beyond six months.</p> <p>High dropout rate and small overall weight loss show that adherence was relatively low in both groups.</p> <p>This study proves a principle and does not provide clinical guidance given the known benefits of fat restriction.</p> <p>As compared with white subjects, black subjects had smaller overall weight loss.</p>
Generalizability- the extent to which the results might apply outside the study	Results may be used to devise weight loss plans for obese individuals.

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Discussion points	<p>Severely obese subjects with prevalence of diabetes and metabolic syndrome lost more weight in a six month period on a CHO restricted diet than on a fat and calorie restricted diet.</p> <p>The greater weight loss in the low CHO group suggests a greater reduction in overall caloric intake rather than a direct effect of macronutrient composition.</p> <p>Possible explanations: Subjects may have experienced greater satiety with liberal portions of protein and fat. Simplicity of the diet Improved compliance due to novelty of the diet.</p> <p>The low CHO diets improved triglycerides for all; insulin sensitivity for non diabetics; glycemic control for diabetics.</p> <p>Amount of weight loss had a significant effect on the degree of improvement in metabolic factors. 5% weight loss on a CHO restricted diet had better metabolic results than those who lost a similar amount of weight while on a fat and calorie restricted diet.</p> <p>Cannot definitely conclude that CHO restriction alone accounted for metabolic improvements in triglycerides and insulin sensitivity. Other uncontrolled variables such as types of CHO – proportion of complex CHO or ratio of CHO to fibre or other unknown variables may have contributed to this effect. Subjects on hypoglycaemic and lipid lowering medication may have confounded results but also allowed inclusion of subjects with obesity related medical disorders typically encountered in clinical practice.</p> <p>High drop-out rate reflected the baseline motivation to lose weight rather than a response to dietary intervention.</p>
Were study limitations discussed?	<p>High level of dropouts early in the study. Attrition rates may reflect the base-line motivation to lose weight rather than response to dietary intervention.</p> <p>Overall weight loss relative to the subjects' severe obesity was small and it was unclear if benefits of carbohydrate-restricted diets extend beyond six months.</p> <p>High dropout rate and small overall weight loss demonstrate that dietary adherence was relatively low in both diet groups.</p>
Future Implications discussed	<p>As compared with white subjects, black subjects had smaller overall weight loss. Future studies should explore if results could be affected by culturally sensitive dietary counselling.</p> <p>This study proves a principle and does not provide clinical guidance given the known benefits of fat-restriction. Future studies evaluating long-term cardiovascular outcomes are needed before a carbohydrate-restricted diet can be endorsed.</p>

APPENDIX A 13: Data Collection Sheets- Shai et al. (2008)

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Author	Shai et al. (2008)
Title	Weight Loss with a Low-Carbohydrate, Mediterranean, or Low-fat Diet
Journal	The New England Journal of Medicine
Quality of Journal and competence of Researchers	Peer Reviewed Journal. Majority of Authors MDs and PhDs.
General Aim Clear	To test the longer term effectiveness and safety of weight-loss diets.
Specific Study objectives stated	To compare the effectiveness and safety of three nutritional protocols: a low fat restricted-calorie diet; a Mediterranean restricted calorie diet and a low-carbohydrate, non-restricted-calorie diet.
Aim and study objectives relevant to research question being explored External Validity - relevance of this particular piece of work to the issue under scrutiny	Relevant to primary research question as to whether the macronutrient composition of a diet, particularly carbohydrate (CHO) manipulation is significant to weight management and cardiovascular disease (CVD) risk management. The inclusion of a restricted low-carbohydrate diet is of particular interest due to potential ease of application. A low-carbohydrate Atkins type diet with no calorie restriction to a low-fat diet and Mediterranean diet plan where calories were restricted to 1500kcal for women and 1800 kcal for men.
Internal Validity - methods and actual results in the light of study objectives	Randomized Controlled Trial, Comparative Intervention.
Study described as randomised	Yes. 322 moderately obese subjects were randomly assigned to one of three diets: low-fat, restricted calorie (LF); Mediterranean restricted calorie diet (MED) or low-carbohydrate non-restricted-calorie diet (LC). The participants were randomly assigned within strata of sex, age (below or above the median), BMI (below or above the median), history of coronary heart disease (yes or no), history of type 2 diabetes (yes or no), and current use of statins (none, <1 year, or ≥1 year) with the use of Monte Carlo simulations.
Study described as double blind	No
Description of withdrawals and dropouts present	Detailed table available to explain withdrawals and dropouts Low- carb diet: 109 assigned, 105 completed 6months (4 withdrew because of disappointment with diet, 102 completed 12m of intervention, 3 left because of lack of motivation and personal reasons, 89 completed 18m of intervention, 13 withdrew of which 6 lacked motivation and 7 had personal reasons; 85 completed 24m of intervention 4 left of which 3 lacked motivation and 1 had personal reasons. 93 of 109 assigned to Mediterranean diet completed the intervention and 94 of those assigned to low-fat diet completed the intervention

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Randomisation / blinding appropriate	Randomisation considered appropriate. Blinding was not appropriate. In order to maintain equal intensity of treatment, the workshop format and the quality of materials were similar across the groups except for instructions and materials specific to each diet strategy
Target Population	Overweight and Obese 40-65 year old Adults with the risk or presence of CVD.
Why was study done? What was perceived general importance?	To conduct a longer term study to study adherence to and effectiveness of 3 nutritional protocols a low fat restricted calorie diet, a Mediterranean restricted calorie diet and a low-carbohydrate Atkins type, non-restricted calorie diet.
Is there a clear hypothesis and objectives?	Not clearly stated but implied
What specific question is being addressed?	Whether low-carbohydrate Atkins type diets and /or Mediterranean diets are as effective and safe as low-fat diets.
The study setting- where did study take place?	Study conducted between July 2005 and June 2007 in Dimona, Israel, in a workplace at a research centre with an on-site medical clinic.
Group actually studied	Mostly Men. (86%). Study conducted in a workplace in Israel at a research centre with an on-site medical clinic.
The social, cultural, economic, ethnic background	Overweight and obese Israeli Men in a workplace setting with food sources available readily in the right form via a workplace cafeteria working closely with dieticians.
Study Approval	The study was approved and monitored by the human subjects committee of Soroka Medical Centre and Ben-Gurion University. Each participant provided written informed consent.
Was there clear inclusion and exclusion criteria and explanations of patient drop out?	The criteria for eligibility were an age of 40 to 65 years and a body-mass index (BMI, the weight in kilograms divided by the square of the height in meters) of at least 27, or the presence of type 2 diabetes (according to the American Diabetes Association criteria) or coronary heart disease, regardless of age and BMI. Persons were excluded if they were pregnant or lactating, had a serum creatinine level of 2 mg per decilitre (177 µmol per litter) or more, had liver dysfunction, had active cancer, or were participating in another diet trial.
Is there a power calculation to determine sample size?	The researchers calculated for a mean (\pm SD) difference between groups of at least 2 ± 10 kg of weight loss, with 100 participants per group and a type I error of 5%; the study had the power to detect significant differences in weight loss of greater than 90%.
Was there selection bias?	Selection bias possible but unlikely. Limited information about application and recruitment process. More detailed exclusion criteria available. Participants received no financial compensation or gifts.

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Was there funding bias?	Study partly supported by the Dr Robert C and Veronika Atkins Research Foundation so there is potentially a funding bias, however no conflict of interest relevant to article was reported.
Confounding Factors	Potentially the significant increase in activity levels over the duration of the intervention.
How does the study group relate to researchers interest groups / patients?	The researcher's interest groups would potentially include overweight and/or obese adults.
What was the intervention and how was it carried out?	<p>The members of each of the three diet groups were assigned to subgroups of 17 to 19 participants, with six subgroups for each group.</p> <p>Each diet group was assigned a registered dietician who led all six subgroups of that group. The dieticians met with their groups in weeks 1, 3, 5, and 7 and thereafter at 6-week intervals, for a total of 18 sessions of 90 minutes each.</p> <p>In order to maintain equal intensity of treatment, the workshop format and the quality of the materials were similar among the three diet groups, except for instructions and materials specific to each diet strategy.</p> <p>Six times during the 2-year intervention, another dietician conducted 10-to-15-minute motivational telephone calls with participants who were having difficulty adhering to the diets and gave a summary of each call to the group dietician.</p> <p>In addition, a group of spouses received education to strengthen their support of the participants</p> <p>Low-Fat Diet- The low-fat, restricted-calorie diet was based on American Heart Association 20 guidelines. The target energy intake was 1500 kcal per day for women and 1800 kcal per day for men, with 30% of calories from fat, 10% of calories from saturated fat, and an intake of 300 mg of cholesterol per day. The participants were counselled to consume low-fat grains, vegetables, fruits, and legumes and to limit their consumption of additional fats, sweets, and high-fat snacks.</p> <p>Mediterranean Diet- The moderate-fat, restricted-calorie, Mediterranean diet was rich in vegetables and low in red meat, with poultry and fish replacing beef and lamb. The target energy intake was 1500 kcal per day for women and 1800 kcal per day for men, with a goal of no more than 35% of calories from fat; the main sources of added fat were 30 to 45 g of olive oil and a handful of nuts (five to seven nuts, <20 g) per day.</p> <p>Low-Carbohydrate Diet- The low-carbohydrate, non-restricted-calorie diet aimed to provide 20 g of carbohydrates per day for the 2-month induction phase and immediately after religious holidays, with a gradual increase to a maximum of 120 g per day to maintain the weight loss. The intakes of total calories, protein, and fat were not limited. However, the participants were counselled to choose vegetarian sources of fat and protein and to avoid trans fat. The diet was based on the Atkins diet.</p>

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What was the intervention and how was it carried out? contd.	<p>A dietician worked closely with the kitchen staff to adjust specific food items to specific diet groups. Each food item was provided with a label showing the number of calories and the number of grams of carbohydrates, fat, and saturated fat, according to an analysis based on the Israeli nutritional database.</p> <p>Each food item was also labelled with a full circle (indicating “feel free to consume”) or a half circle (indicating “consume in moderation”). The labels were colour-coded according to diet group and were updated daily</p>
What was measured and how was it measured?	<p>Adherence to the diets was evaluated by a validated food-frequency questionnaire 24 that included 127 food items and three portion-size pictures for 17 items.</p> <p>A subgroup of participants completed two repeated 24-hour dietary recalls to verify absolute intake.</p> <p>A validated questionnaire was used to assess physical activity.</p> <p>At baseline and at 6, 12, and 24 months of follow-up, the questionnaires were self-administered electronically through the workplace intranet.</p> <p>The electronic questionnaire helped to ensure completeness of the data by prompting the participant when a question was not answered and it permitted rapid automated reporting by the group dieticians.</p> <p>The participants were weighed without shoes to the nearest 0.1 kg every month. With the use of a wall-mounted stadiometer, height was measured to the nearest millimetre at baseline for determination of BMI.</p> <p>Waist circumference was measured halfway between the last rib and the iliac crest.</p> <p>Blood pressure was measured every 3 months with the use of an automated system (Datascop Acutor 4) after 5 minutes of rest.</p> <p>Blood samples were obtained by venipuncture at 8 a.m. after a 12-hour fast at baseline and at 6, 12, and 24 months and were stored at –80°C until an assay for lipids, inflammatory biomarkers, and insulin could be performed.</p> <p>Levels of fasting plasma glucose, glycated haemoglobin, and liver enzymes were measured in fresh samples. Serum levels of total cholesterol, high-density-lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides were determined enzymatically with a Wako R-30 automatic analyzer.</p> <p>Plasma insulin levels were measured with the use of an enzyme immunometric assay.</p> <p>Plasma levels of high-molecular-weight adiponectin were measured by an enzyme-linked immunosorbent assay (ELISA).</p>

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What was measured and how was it measured? contd.	<p>Plasma leptin levels were assessed by ELISA.</p> <p>Plasma levels of high-sensitivity C-reactive protein were measured by ELISA.</p> <p>For weight loss, the pre-specified primary aim was the change in weight from baseline to 24 months.</p> <p>The study analyzed the dietary-composition data and biomarkers with the use of raw unadjusted means, without imputation of missing data.</p>
Were baseline measures used?	<p>The mean age was 52 years and the mean BMI was 31. Most participants (86%) were men.</p> <p>At baseline, there were no significant differences in the composition of the diets consumed by participants assigned to the low-fat, Mediterranean, and low-carbohydrate diets.</p>
Were process measures used?	<p>The clinic and laboratory staff members were unaware of the treatment assignments, and the study coordinators were unaware of all outcome data until the end of the intervention.</p> <p>Statistics: Dietary-intake values were compared between groups at each time point with the use of an analysis of variance in which all pairwise comparisons among the three diet groups were performed with the use of Tukey's Studentized range test.</p> <p>For intention-to-treat analyses, all 322 participants were included and the most recent values for weight and blood pressure were used.</p> <p>To evaluate the repeated measurements over time, generalized estimating equations for panel data analysis were used also known as cross-sectional time-series analysis.</p> <p>The within person changes from baseline in each diet group was determined with the use of pairwise comparisons.</p> <p>The homeostasis model assessment of insulin resistance (HOMA-IR) was calculated according to the following equation: $\text{insulin (U/ml)} \times \text{fasting glucose (mmol/litre)} \div 22.5$.</p> <p>SPSS software, version 15, and Stata software, version 9, was used for the statistical analysis.</p>
Were outcome measures identified? Are there clear validated outcomes?	<p>Yes.</p>

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Are the methods quantitative or qualitative?	Both qualitative and quantitative.
Safety Results	The proportion of participants with detectable urinary ketones at 24 months was higher in the low-carbohydrate group (8.3%) than in the low-fat group (4.8%) or the Mediterranean-diet group (2.8%) (P = 0.04).
Endpoint/ Biomarker Tested	Adherence, dietary intake, energy expenditure, weight loss, lipid profiles, CRP, adiponectin, leptin, blood sugar and insulin markers, liver function
Are there end points other than those reported that might be relevant and important	Apo lipoprotein a and b; bone and kidney health as one study arm was the Atkins diet.
Are the endpoints relevant to actual practice	Yes.
Dietary Intake and Adherence Results	<p>The overall rate of adherence was 95.4% at 12 months and 84.6% at 24 months.</p> <p>The 24-month adherence rates were 90.4% in the low-fat group, 85.3% in the Mediterranean diet group, and 78.0% in the low-carbohydrate group (P = 0.04 for the comparison among diet groups).</p> <p>Daily energy intake as assessed by the food-frequency questionnaire, decreased significantly at 6, 12, and 24 months in all diet groups as compared with baseline (P<0.001); there were no significant differences among the groups in the amount of decrease.</p> <p>The low-carbohydrate group had a lower intake of carbohydrates (P<0.001) and higher intakes of protein (P<0.001), total fat (P<0.001), saturated fat (P<0.001), and total cholesterol (P = 0.04) than the other groups.</p> <p>The Mediterranean- diet group had a higher ratio of monounsaturated to saturated fat than the other groups (P<0.001) and a higher intake of dietary fibre than the low-carbohydrate group (P = 0.002).</p> <p>The low-fat group had a lower intake of saturated fat than the low-carbohydrate group (P = 0.02).</p>
Weight loss and cardio-protective and other mechanisms identified,	<p>Adherence to diet and calorie deficit.</p> <p>Individualisation of diets to personal preferences and metabolic needs.</p>

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<p>Weight Loss / Body Composition results</p>	<p>The mean weight changes among the 272 participants who completed 24 months of intervention were -3.3 ± 4.1 kg in the low-fat group, -4.6 ± 6.0 kg in the Mediterranean-diet group, and -5.5 ± 7.0 kg in the low-carbohydrate group ($P = 0.03$ for the comparison between the low-fat and the low-carbohydrate groups at 24 months).</p> <p>The mean (\pmSD) changes in BMI were -1.0 ± 1.4 in the low-fat group, -1.5 ± 2.2 in the Mediterranean-diet group, and -1.5 ± 2.1 in the low-carbohydrate group ($P = 0.05$ for the comparison among groups).</p> <p>All groups had significant decreases in waist circumference and blood pressure, but the differences among the groups were not significant. The waist circumference decreased by a mean of 2.8 ± 4.3 cm in the low-fat group, 3.5 ± 5.1 cm in the Mediterranean-diet group, and 3.8 ± 5.2 cm in the low-carbohydrate group ($P = 0.33$ for the comparison among groups).</p>
<p>Cardiac Risk Factor Results</p>	<p>Systolic blood pressure fell by 4.3 ± 11.8 mm Hg in the low-fat group, 5.5 ± 14.3 mm Hg in the Mediterranean-diet group, and 3.9 ± 12.8 mm Hg in the low-carbohydrate group ($P = 0.64$ for the comparison among groups). The corresponding decreases in diastolic pressure were 0.9 ± 8.1, 2.2 ± 9.5, and 0.8 ± 8.7 mm Hg ($P = 0.43$ for the comparison among groups).</p> <p>HDL cholesterol increased during the weight-loss and maintenance phases in all groups, with the greatest increase in the low-carbohydrate group (8.4 mg per decilitre [0.22 mmol per litre], $P < 0.01$ for the interaction between diet group and time), as compared with the low-fat group (6.3 mg per decilitre [0.16 mmol per litre]).</p> <p>Triglyceride levels decreased significantly in the low-carbohydrate group (23.7 mg per decilitre [0.27 mmol per litre], $P = 0.03$ for the interaction between diet group and time), as compared with the low-fat group (2.7 mg per decilitre [0.03 mmol per litre]).</p> <p>LDL cholesterol levels did not change significantly within groups, and there were no significant differences between the groups in the amount of change.</p> <p>Overall, the ratio of total cholesterol to HDL cholesterol decreased during both the weight-loss and the maintenance phases. The low-carbohydrate group had the greatest improvement, with a relative decrease of 20% ($P = 0.01$ for the interaction between diet group and time), as compared with a decrease of 12% in the low-fat group.</p> <p>The level of high-sensitivity C-reactive protein decreased significantly ($P < 0.05$) only in the Mediterranean- diet group (21%) and the low-carbohydrate group (29%), during both the weight-loss and the maintenance phases, with no significant differences among the groups in the amount of decrease.</p>

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<p>Endocrine markers and Hormonal Effects</p>	<p>During both the weight-loss and the maintenance phases, the level of high molecular-weight adiponectin increased significantly ($P<0.05$) in all diet groups, with no significant differences among the groups in the amount of increase.</p> <p>Circulating leptin, which reflects body-fat mass, decreased significantly ($P<0.05$) in all diet groups, with no significant differences among the groups in the amount of decrease. The decrease in leptin paralleled the decrease in body weight during the two phases. The interaction between the effects of low- carbohydrate diet and sex on the reduction of leptin ($P = 0.04$), as compared with the low-fat diet, reflects the greater effect of the low-carbohydrate diet among men.</p> <p>Among the 36 participants with diabetes, only those in the Mediterranean-diet group had a decrease in fasting plasma glucose levels (32.8 mg per decilitre); this change was significantly different from the increase in plasma glucose levels among participants with diabetes in the low-fat group ($P<0.001$ for the interaction between diet group and time). There was no significant change in plasma glucose level among the participants without diabetes ($P<0.001$ for the interaction among diabetes and Mediterranean diet and time).</p> <p>In contrast, insulin levels decreased significantly in participants with diabetes and in those without diabetes in all diet groups, with no significant differences among groups in the amount of decrease.</p> <p>Among the participants with diabetes, the proportion of glycated haemoglobin at 24 months decreased by $0.4\pm1.3\%$ in the low-fat group, $0.5\pm1.1\%$ in the Mediterranean-diet group, and $0.9\pm0.8\%$ in the low-carbohydrate group. The changes were significant ($P<0.05$) only in the low-carbohydrate group ($P = 0.45$ for the comparison among groups).</p> <p>Liver-Function Tests Changes in bilirubin, alkaline phosphatase, and alanine aminotransferase levels were similar among the diet groups. Alanine aminotransferase levels were significantly reduced from baseline to 24 months in the Mediterranean-diet and the low-carbohydrate groups (reductions of 3.4 ± 11.0 and 2.6 ± 8.6 units per litre, respectively; $P<0.05$ for the comparison with baseline in both groups).</p>
<p>Exercise and Medication use</p>	<p>The amount of physical activity increased significantly from baseline in all groups with no significant difference among the groups in the amount of increase. The energy expenditure increase may be a potential confounding factor in assessing weight loss and or CVD marker results over the period of the intervention.</p> <p>During the study, there was little change in usage of medications, and there were no significant differences among groups in the amount of change. Four participants initiated and three stopped cholesterol-lowering therapy. Twenty participants initiated blood-pressure treatment, five initiated medications for glycemic control, and one reduced the dosage of medications for glycemic control.</p>
<p>What effect may bias have on the result?</p>	<p>Atkins Foundation support may have influenced aiming for a favourable result for the low-carbohydrate diet.</p>

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<p>The Author's conclusions - are these justified?</p>	<p>This 2-year dietary-intervention study, found that the Mediterranean and low-carbohydrate diets are effective alternatives to the low-fat diet for weight loss and appear to be just as safe as the low-fat diet.</p> <p>In addition to producing weight loss in this moderately obese group of participants, the low-carbohydrate and Mediterranean diets had some beneficial metabolic effects, a result suggesting that these dietary strategies might be considered in clinical practice and that diets might be individualized according to personal preferences and metabolic needs.</p>
<p>Generalizability- the extent to which the results might apply outside the study</p>	<p>The unique nature of the workplace in this study, which permitted a closely monitored dietary intervention for a period of 2 years, makes it difficult to generalize the results to other free living populations. However, the researchers recognize that similar strategies to maintain adherence could be applied elsewhere and that this intervention model may be useful to apply in a corporate sponsored workplace initiative.</p>
<p>Discussion points</p>	<p>The similar caloric deficit achieved in all diet groups suggests that a low-carbohydrate, non-restricted-calorie diet may be optimal for those who will not follow a restricted-calorie dietary regimen.</p> <p>The increasing improvement in levels of some biomarkers over time up to the 24-month point, despite the achievement of maximum weight loss by 6 months, suggests that a diet with a healthful composition has benefits beyond weight reduction.</p> <p>The strengths of the study include the one phase design, in which all participants started simultaneously; the relatively long duration of the study; the large study-group size; and the high rate of adherence.</p> <p>The monthly measurements of weight permitted a better understanding of the weight-loss trajectory than was the case in previous studies.</p> <p>Two phases of weight change were observed - initial weight loss and weight maintenance. The maximum weight reduction was achieved during the first 6 months; this period was followed by the maintenance phase of partial rebound and a plateau. Among all diet groups, weight loss was greater for those who completed the 24-month study than for those who did not.</p> <p>Hence even moderate weight loss has health benefits, and this study suggests benefits of behavioural approaches that yield weight losses similar to those obtained with pharmacotherapy.</p> <p>The changes observed in levels of adiponectin and leptin, which were consistent in all groups, reflect loss of weight.</p> <p>Changes in levels of various biomarkers were noted (leptin, adiponectin, and high-sensitivity C-reactive protein) that are apparently related to loss of adipose tissue and changes in biomarkers (triglycerides, HDL cholesterol, glucose, and insulin) that apparently reflect, in part, the effects of specific diet composition.</p> <p>Consumption of monounsaturated fats is thought to improve insulin sensitivity, an effect that may explain the favourable effect of</p>

APPENDIX A 13: Data Collection Sheets- Shai et al. (2008)

(Some text and/or data extracted verbatim from study article for many of the descriptive sections. Figure, Table and Numerical references included in brackets refer to the original article).

Discussion points- Contd.	<p>the Mediterranean diet on glucose and insulin levels.</p> <p>The results imply that dietary composition modifies metabolic biomarkers in addition to leading to weight loss.</p> <p>The results suggest that health care professionals might consider more than one dietary approach, according to individual preferences and metabolic needs, as long as the effort is sustained.</p> <p>This trial also suggests a model that might be applied more broadly in the workplace, using the employer as a health coach could be a cost-effective way to improve health.</p> <p>The use of dietary group sessions, spousal support, food labels, and monthly weighing in the workplace within the framework of a health promotion campaign might yield weight reduction and long-term health benefits.</p>
Were study limitations discussed?	<p>Few women were enrolled however the researchers we observed a significant interaction between the effects of diet group and sex on weight loss (women tended to lose more weight on the Mediterranean diet), and this difference between men and women was also reflected in the changes in leptin levels. This possible sex-specific difference should be explored in further studies.</p> <p>The researchers recognize that measurement of HOMA-IR is not an optimal method to assess insulin resistance among persons with diabetes.</p>
Future Implications discussed	<p>This study highlights a model that might be applied more broadly in the workplace and the concept of the Employer as a health coach as suggested by Okie (2007). Also using dietary group sessions, spousal support, food labels and monthly weighing in the workplace might be pragmatic suggestions for weight reduction and long term health benefits.</p>

APPENDIX A 14: Data Collection Sheets – Stern et al. (2004)

(Some text and/or data extracted verbatim from study article for many of the descriptive sections. Figure, Table and Numerical references included in brackets refer to the original article).

Author	Stern et al. (2004)
Title	The Effects of Low-Carbohydrate versus Conventional weight Loss Diets in Severely Obese Adults: One year follow-up of a randomized trial
Journal	Annals of Internal Medicine
Quality of Journal and competence of Researchers	Peer Reviewed Journal. 4 out of 9 authors are MDs.
General Aim Clear	To follow up on a previously conducted 6 month trial to assess the long term effects of a low carbohydrate diet LC versus a conventional fat and calorie reduced diet.
Specific Study objectives stated	To review the one year outcomes between the 2 diets as a follow up to the trial conducted by Samaha et al. (2003).
Aim and study objectives relevant to research question being explored External Validity - relevance of this particular piece of work to the issue under scrutiny	Relevant to primary research question as to whether the macronutrient composition of a diet and particularly CHO restriction is significant to weight management and CVD risk management. A longer-term view of a low-carbohydrate Atkins type diet compared with a low-fat conventional diet for severely obese group of subjects. Follow-up to Samaha et al. (2003).
Internal Validity - methods and actual results in the light of study objectives	Randomized trial. Comparative intervention
Study described as randomised	As for Samaha et al. (2003). Random assignment of subjects to one of two diets.
Study described as double blind	No
Description of withdrawals and dropouts present	Of the 132 enrolled persons, follow-up was done at 6 months for 79 persons and at 1 year for 87 persons. For measurements at 6 months, we retrieved weights on an additional 16 persons on the low-carbohydrate diet and 23 persons on the conventional diet (total, 39 persons at a mean [\pm SD] of 6.6 ± 1.2 months). For measurements at 1 year, we retrieved weights on 18 persons on the low-carbohydrate diet and 21 persons on the conventional diet (total, 39 persons at a mean [\pm SD] of 13.5 ± 3.2 months). Thus, we had 6-month weights on 118 of 132 persons (89%) and 1-year weights on 126 of 132 persons (96%). Of the 18 persons who missed the 6-month visit but returned for the 1-year visit (6 in the low-carbohydrate group and 12 in the conventional diet group), all but 2 had 6-month weights retrieved from medical records. Of the 6 persons for whom no 1-year weights were available, 2 were in the low-carbohydrate group and 4 in the conventional diet group.

APPENDIX A 14: Data Collection Sheets – Stern et al. (2004)

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Randomisation / blinding appropriate	Randomisation appropriate ; Blinding not relevant
Target Population	Severely obese Adults
Why was study done? What was perceived general importance?	To assess the sustainability of results attained during a previous study –Samaha et al. 2003.
Is there a clear hypothesis and objectives?	Yes. That severely obese subjects with a high prevalence of diabetes or the metabolic syndrome would have greater weight loss without detrimental effects on risk factors for atherosclerosis while on a carbohydrate-restricted diet than on a calorie and fat-restricted low-fat diet
What specific question is being addressed?	For severely obese individuals, do low-carbohydrate diets work better than conventional low-fat, low-calorie diets and is the weight loss sustainable over the longer term of one year.
The study setting- where did study take place?	Philadelphia Veterans Affairs Medical Center
The study population - Intended group to whom results should apply vs. group actually studied	Participants were recruited from the outpatient practices of the Philadelphia Veterans Affairs Medical Center and included persons 18 years of age and older with a body mass index (BMI) of 35 kg/m ² or greater.
Group actually studied	Between May 2001 and November 2001, 132 persons were randomly assigned to either a low-carbohydrate diet (<i>n</i> = 64) or a conventional diet (<i>n</i> = 68).
The social, cultural, economic, ethnic background	Veterans. A high proportion of black subjects
Study Approval	The Institutional Review Committee at the Philadelphia Veterans Affairs Medical Center approved the study, and all participants provided written informed consent.
Was there clear inclusion and exclusion criteria and explanations of patient drop out?	Study included persons 18 years of age and older with a body mass index (BMI) of 35 kg/m ² or greater. The exclusion criteria were a serum creatinine level greater than 133 μ mol/L (>1.5 mg/dL), hepatic disease, severe life-limiting medical illness, inability to self-monitor glucose levels, or active use of a weight loss program or weight loss medication. 20 persons on the low CHO diet and 25 on the conventional diet dropped out by 1 year
Is there a power calculation to determine sample size?	Assuming a two-sided type 1 error of 5% the authors estimated a need for 100 subjects for the study to have 80% power to demonstrate a mean \pm SD weight loss that was 5 \pm 12v kg greater in the low CHO group than the low fat group. A dropout rate of 25 was anticipated so the enrolment target was 135.

APPENDIX A 14: Data Collection Sheets – Stern et al. (2004)

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Was there selection bias?	None evident.
Was there funding bias?	None evident. The funding source had no role in the design, conduct, or reporting of the study or in the decision to submit the manuscript for publication.
Confounding Factors	Many of the subjects were taking lipid lowering medication and hypoglycaemic agents.
How does the study group relate to researchers interest groups / patients?	Obese and severely obese subjects with evidence of metabolic disease fall in the scope of the researchers interests.
What was the intervention and how was it carried out?	Counselling sessions continued for 11 months – 5 months after the end of 6 month trial.
What was measured and how was it, measured?	Changes in weight, lipid levels, glycemic control and insulin sensitivity.
Were baseline measures used?	<p>Participants were well matched between diet groups regarding baseline characteristics, although the low-carbohydrate group had more hypertensive and white persons (Table 1). Both groups had a high prevalence of diabetes or the metabolic syndrome (Table 1). Twenty persons on the low-carbohydrate diet and 25 on the conventional diet dropped out by 1 year. These persons were younger and had a lower prevalence of sleep apnea but were not otherwise significantly different from those who completed the study (Table 1).</p> <p>Differences in baseline lipid values ($P > 0.2$ for all comparisons), diet composition ($P \geq 0.149$ for all comparisons), glycemic control indices ($P \geq 0.158$ for all comparisons), and insulin sensitivity ($P > 0.2$) between those who dropped out of the study and those who completed the study were not significant.</p>
Were process measures used?	<p>Changes in weight, dietary intake and metabolic data were compared between the 2 diets by random-coefficient analysis to allow for a variable number of observations for participants and to take account that the repeated observations of the outcome variables over time for individuals were correlated.</p> <p>A restricted maximum likelihood analysis was used which assumed that changes were distributed according a bivariate normal distribution and that data were missing at random.</p> <p>Missing data : Of the 132 enrolled persons, follow up was done at 6months for 79 persons and at 1 year for 87 persons. Of the 18 persons who missed the 6 month visit (6 in the low CHO group and 12 in the low fat group, 6 month weights were retrieved for all but 2 subjects in the low CHO group from medical records.</p> <p>Of the 4 subjects in the low fat group and 2 in the low CHO group for whom 1 year weights were not available, these were retrieved from medical records though these may be subject to error as the scales used and clothing protocol would have differed from the</p>

APPENDIX A 14: Data Collection Sheets – Stern et al. (2004)

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Were process measures used? contd.	<p>study.</p> <p>We used several approaches to handle the 45 participants with missing data for diet recall and metabolic measurements. For the primary analysis by random-coefficient analysis, we assumed data were missing at random. To verify this assumption, we performed sensitivity analyses based on comparisons of baseline characteristics and weight loss differences between those who dropped out and those who completed the study. We also performed 2 additional sensitivity analyses: The first analysis included only persons who completed the study, and the second analysis included all persons, with the baseline data carried forward for those persons who dropped out.</p>
Were outcome measures identified? Are there clear validated outcomes?	<p>Weight, self reported medical history and blood pressure at baseline, 6 months and 1 year. Blood glucose, glycosylated haemoglobin, serum lipids, blood pressure.</p> <p>Primary end point was total weight loss at 1 year.</p> <p>Secondary analyses included changes from baseline of serum lipids, insulin sensitivity and glycemic control and dietary intake.</p>
Are the methods quantitative or qualitative?	Quantitative and qualitative.
Safety Results	<p>2 persons on the low-CHO diet and 4 on the conventional diet developed diabetes at 1 year.</p> <p>Blood urea nitrogen levels increased more in the low CHO group but changes in uric acid levels were not clinically significant. 3 individuals on the low CHO group died during the study but these were not regarded as diet related.</p>
Endpoint/ Biomarker Tested	Weight loss, serum lipids, glycemic control and insulin sensitivity, BP, adverse reactions, attrition, assessment of dietary intake.
Are there end points other than those reported that might be relevant and important	Apolipoprotein a and b, renal and bone health as one arm was a ketogenic diet.
Are the endpoints relevant to actual practice	Yes and consistent with other studies.
Dietary Intake and Adherence Results	<p>Caloric intake decreased more by year 1 in the low CHO group than in the LF group. The low CHO group reduced CHO by 52%, reduced fibre intake BY 42 %, increased total fat intake by 31%; increased dietary cholesterol intake by 21%, reduced sodium intake by 21% relative to baseline.</p> <p>20 persons on the low CHO diet and 25 on the conventional diet dropped out by 1 year</p>

APPENDIX A 14: Data Collection Sheets – Stern et al. (2004)

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Weight loss and cardio-protective mechanisms identified	<p>Although it has been speculated that a low-carbohydrate diet would facilitate weight loss by promoting the metabolism of adipose tissue (13), our data suggest that weight loss differences may be explained by lower caloric intake on a low-carbohydrate diet.</p> <p>If true, this may be attributable to the simplicity of a low-carbohydrate diet or to greater effects on satiety. Of note, persons on the low-carbohydrate diet who dropped out of the study were less likely to lose weight, whereas those assigned to the conventional diet lost a similar amount of weight whether or not they remained in the study.</p> <p>This observation, together with the difference between diets in weight loss beyond 6 months, raises the possibility that a low-carbohydrate diet is less sustainable than a conventional diet.</p> <p>Despite modest and comparable overall weight loss, the responses of triglycerides and HDL cholesterol to the low-carbohydrate diet were more favorable than to the conventional diet. These findings are consistent with previous studies (7, 14–17) and may be related to diminished very-low-density lipoprotein triglyceride production by the liver in response to decreased carbohydrate substrate delivery, as well as to improvements in insulin sensitivity. The greater preservation of HDL cholesterol on the low-carbohydrate diet may be a secondary effect of the greater decrease in triglycerides via cholesterol ester transferase or through down regulation of hepatic scavenger receptor B1 levels (18). The expression of these receptors, which bind HDL cholesterol and facilitate reverse cholesterol transport to the liver, may be modulated by dietary fats (18).</p>
Weight Loss / Body Composition results	<p>Participants on the low CHO diet maintained most of their 6 month weight loss whereas those on the conventional diet continued to lose weight throughout the year. The final 1 year weight change was $-5 \pm 8.7\text{kg}$ in the low CHO group and $-3.1 \pm 8.4\text{kg}$ in the conventional diet group. The difference between the two diet groups was not significant.</p> <p>Persons on the low-CHO diet who dropped out lost less weight than those who completed the study. In contrast weight loss was not significantly different for those on the conventional diet.</p>
Ketonuria Results	None reported.
Cardiac Risk Factor Results	<p>Changes in total and LDL cholesterol were not significantly different between groups.</p> <p>Triglyceride levels decreased more in the low CHO group than in the conventional diet group ($P=0.044$ before and $P=0.041$ after adjustment for baseline variables. A separate sensitivity analysis that included only the 87 persons who completed the study confirmed this finding. Assignment to the low CHO group and greater weight loss were each independent predictors of a decrease in triglyceride concentration suggesting a direct effect of the low CHO diet on triglyceride reduction.</p> <p>The HDL cholesterol concentration decreased more in the conventional diet group than in the low-CHO group ($P=0.025$ before and $P=0.014$ after adjusting for baseline variables. The results indicated a direct diet-related effect on HDL cholesterol.</p>

APPENDIX A 14: Data Collection Sheets – Stern et al. (2004)

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Hormonal & Endocrine Results	<p>Glycemic Control and Insulin Sensitivity The difference between the 2 diet groups was not significant. Glycosylated haemoglobin in the small group with diabetes (n=54) decreased more in the low-CHO group after adjusting for baseline differences. The results show a direct effect of the low CHO diet on glycemic control</p>
Exercise and Medication use	<p>Many subjects were taking lipid-lowering medications and hypoglycaemic agents. No comment on exercise.</p>
What effect may bias have on the result?	<p>None noted.</p>
The Author's conclusions - are these justified?	<p>Similar weight loss in persons randomly assigned to a low CHO diet or a conventional diet by 1 year. Modest overall weight loss on both diet groups. Assignment to the low CHO group had a direct and more favourable effect on triglyceride level, HDL cholesterol level and glycemic control in the smaller diabetic subset.</p> <p>Findings give further evidence that restriction of CHO in obese persons who may be overconsuming CHO at baseline may have favourable metabolic effects.</p> <p>Caution is still needed in recommending a low-CHO diet as important concerns remain.</p>
Generalizability- the extent to which the results might apply outside the study	<p>Results may be used to devise weight loss plans for obese individuals.</p>
Discussion points	<p>A larger study might have shown a statistically significant difference in weight loss.</p> <p>The enrolment targets were based on a maximum anticipated weight loss by 6 months and assumed weight stabilization thereafter. As weight loss continued beyond 6 months in the conventional diet group a sample size of 284 persons per group may have been more appropriate to show a difference between the groups at 1 year.</p> <p>In contrast to Foster et al. (2003) persons on the low-CHO maintained most of their initial weight loss where as those on the conventional diet continued to lose weight. The difference may be due to more intensive counselling.</p> <p>Data suggests that weight loss differences may be explained by lower caloric intake on a low-CHO diet rather than metabolism of adipose tissue.</p> <p>Possible points in favour of low-CHO diet could be the simplicity and greater effects on satiety.</p>

APPENDIX A 14: Data Collection Sheets – Stern et al. (2004)

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Discussion points contd.	<p>Persons on the low-CHO diet who dropped out were less likely to lose weight whereas those on the conventional diet continued to lose weight whether or not they remained in the study. This observation together with the difference between diets in weight loss beyond six months suggests that a low CHO diet is less sustainable than a conventional diet.</p> <p>The low-CHO diet followed in the study had a healthy lower sodium intake and unhealthy higher fat and cholesterol and lower fibre levels. The difference in sodium intake could represent less consumption of pre-packaged, low-fat but high salt foods in the low-CHO group.</p> <p>The low-CHO diet had more favourable responses of triglycerides and HDL cholesterol consistent with previous studies. This may be related to diminished very-low density lipoprotein (VLDL) triglyceride production by the liver in response to decreased CHO intake and improved insulin sensitivity.</p> <p>The higher HDL cholesterol on the low CHO diet may be a secondary effect of the greater decrease in triglycerides via cholesterol ester transferase or through down regulation of hepatic scavenger receptor B1 levels. The expression of these receptors which bind HD cholesterol and facilitate reverse cholesterol transport to the liver may be modulated by dietary fats.</p> <p>Glycosylated haemoglobin in the small diabetic group improved in the low CHO group. This is regarded as clinically significant to micro and macro vascular complications of diabetes.</p>
Were study limitations discussed?	<p>The weights retrieved from medical records were obtained on scales that were different from those used for the study and were probably obtained in a non-uniform manner with regard to clothing.</p> <p>Overall weight loss was modest.</p> <p>Overall dropout rate was high.</p> <p>The authors tried to minimize biasing effects by extracting 1 year weights for persons who dropped out however these weights were not measured in a standardized manner. Any random measurement errors would bias results towards the null.</p> <p>Most persons did not meet their dietary targets (< 30g of CHO daily in the low CHO group and a reduction of 500kcal per day in the conventional diet. Meeting these targets would have yielded different results.</p> <p>There were differences between persons who completed the study and those who dropped out such as greater weight loss in the former. However observed differences in responses of triglyceride, HDL cholesterol and glycosylated haemoglobin were independent of differences in weight loss.</p> <p>We cannot exclude that a larger study might have demonstrated a statistically significant difference in weight loss between diets.</p>

APPENDIX A 14: Data Collection Sheets – Stern et al. (2004)

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Were study limitations discussed?	Our enrollment targets were based on a maximum anticipated weight loss by 6 months and assumed weight stabilization thereafter. Given that weight loss continued beyond 6 months in the conventional diet group, we would have needed a sample size of approximately 284 persons per group to show a difference between groups at 1 year, assuming preservation of the observed changes.
Future Implications discussed	Future studies will need to evaluate whether a low CHO has more favourable effects on the development of diabetes and on cardiovascular outcomes.

APPENDIX A 15: Data Collection Sheets – Yancy et al. (2004)

(Some text and/or data extracted verbatim from study article for many of the descriptive sections. Figure, Table and Numerical references included in brackets refer to the original article).

Author	Yancy, Olsen, Guyton, Bakst & Westman (2004)
Title	A Low-Carbohydrate, Ketogenic Diet versus a Low-Fat Diet to Treat Obesity and Hyperlipidemia
Journal	Annals of Internal Medicine
Quality of Journal and competence of Researchers	Peer Reviewed Journal. 3 out of 5 of the Authors are MDs. The lead author is an associate professor at Duke University, USA.
General Aim Clear	To ascertain the effectiveness of a low CHO diet in treating obesity and hyperlipidemia.
Specific Study objectives stated	To compare the effects of a low-carbohydrate, ketogenic diet program with those of a low-fat, low cholesterol, reduced – calorie diet
Aim and study objectives relevant to research question being explored External Validity - relevance of this particular piece of work to the issue under scrutiny	Relevant to primary research question as to whether the macronutrient composition of a diet is significant to weight management and CVD risk management. A low-carbohydrate Atkins Diet compared with a low-fat conventional diet.
Internal Validity - methods and actual results in the light of study objectives	Comparative Intervention. Not controlled.
Study described as randomised	Yes. Community dwelling hyperlipidemic persons were randomly assigned to either a low CHO, ketogenic diet or a low-fat , low-cholesterol, reduced calorie diet for 24 weeks
Study described as double blind	No
Description of withdrawals and dropouts present	Yes. One withdrawal in the Low-CHO group who discontinued the study before receiving dietary instruction. In the low-CHO group, 4 (7%) could not keep meeting schedule, 5 (8%) could not adhere to the diet, 1 (2%) was unsatisfied with weight loss, 1 was lost to follow-up, 3 (5%) dropped out due to adverse effects of which 2 had increases in LDL cholesterol and 1 had shakiness and uneasiness. Of 59 – 45 (76%) completed in the low CHO group and of 60 in the low-fat group, 34 (57%) completed. In the low-fat group, 15 participants (25%) could not adhere to meeting schedule, 3(5%) could not adhere to diet, 6(10%) were unsatisfied with weight loss and 2(3%) were lost to follow up

APPENDIX A 15: Data Collection Sheets – Yancy et al. (2004)

(Some text and/or data extracted verbatim from study article for many of the descriptive sections. Figure, Table and Numerical references included in brackets refer to the original article).

Randomisation / blinding appropriate	Randomisation was relevant. Blinding for participants would not be possible as these are popular diets that participants would most likely be aware of.
Target Population	Overweight, , hyperlipidemic individuals
Why was study done? What was perceived general importance?	To address the scarcity of data on the long-term effects of low-CHO diets on body weight, body composition and serum lipid levels
Is there a clear hypothesis and objectives?	The objective is to compare the effects of a low-carbohydrate ketogenic diet with a low-fat, low cholesterol reduced-calorie diet on obesity and lipid control.
What specific question is being addressed?	Long-term efficacy and adverse effects of low-CHO weight reduction diets
The study setting- where did study take place?	Group Meetings took place at an out-patient research clinic
Group actually studied	Generally healthy persons recruited from the community. Of 1051 volunteers screened for eligibility, 120 underwent randomization.
The social, cultural, economic, ethnic background	Generally healthy individuals from the local community (Durham, North Carolina)
Study Approval	All participants provided written informed consent. Study approved by the institutional review board of Duke University Health System.
Was there clear inclusion and exclusion criteria and explanations of patient drop out?	Inclusion criteria: Generally healthy persons were recruited from the community. Inclusion criteria Included: age 18-65 years; BMI – 30-60kg/m ² ; desire to lose weight; elevated lipid levels (total cholesterol level >5.17 mmol/L [>200mg/dL], LDL cholesterol > 3.36mmol/L [> 130mg/dL] or triglycerides level >2.26 mmol/L [>200mg/dL]) and no serious medical condition. Exclusion criteria : use of any prescription medication in the previous 2 months (except for oral contraceptives, estrogen therapy, stable thyroid medication); pregnancy or breastfeeding; use of weight loss or diet pills in previous 6 months; baseline ketonuria.
Is there a power calculation to determine sample size?	None evident.
Was there selection bias?	None evident.
Was there funding bias?	The Study had grant support from the Robert C Atkins Foundation. However the grants received or pending receipt by Westman and Yancy have been declared as potential conflicts of interest - leaving the review process to evaluate if such a conflict is evident. Investigators at Duke University conducted the study and maintained exclusive control of all data and analyses. The funding

APPENDIX A 15: Data Collection Sheets – Yancy et al. (2004)

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Was there funding bias? contd.	source had no involvement in the recruitment of participants; study interventions; collection, analysis, or interpretation of the data; or preparation or review of the manuscript.
Confounding Factors	Nutritional supplementation to one group but not the other
How does the study group relate to researchers interest groups / patients?	Potentially obese individuals with impaired lipid control would be clients of the researcher and the impact of dietary therapy on the endpoints identified would be relevant to the researcher.
What was the intervention and how was it carried out?	<p>Randomized, controlled trial.</p> <p>Low-carbohydrate diet (initially, <20 g of carbohydrate daily) plus nutritional supplementation, exercise recommendation, and group meetings, or low-fat diet (<30% energy from fat, <300 mg of cholesterol daily, and deficit of 500 to 1000 kcal/d) plus exercise recommendation and group meetings.</p> <p>Using computer generated simple randomization lists, participants were allocated to receive the low-CHO diet or the low-fat diet. The intervention included group meetings, diet instruction and an exercise recommendation. Group meetings took place twice monthly for 3 months then monthly for 3 months. Meetings typically lasted one hour and consisted of diet instruction, supportive counselling, questionnaires and biomedical measurements. During the study, the participants selected their own menus and prepared or bought meals according to the guidelines presented to them. Participants encouraged to exercise for 30 minutes at least 3 times weekly but no formal exercise program or incentives were provided.</p> <p>For the Low-CHO Diet Group – using a popular diet book published by a lay press and additional handouts, trained research staff instructed participants to restrict intake of CHO to less than 20g/d. Participants permitted unlimited amounts of animal foods (meat, fowl, fish and shellfish), unlimited eggs, 4 oz of hard cheese, 2 cups of salad vegetables (lettuce, spinach or celery) and 1 cup of low-CHO vegetables (broccoli, cauliflower or squash) daily. Participants encouraged to drink 6-8 glasses of water daily. When participants were halfway to their goal body weight at week 10 visit, they were advised to add approximately 5g of CHO to their daily intake each week till body weight was maintained. To simulate the practice of the study sponsor the low-CHO group received daily nutritional supplements including a multivitamin, essential oils, diet formulation and chromium picolinate.</p> <p>For the Low-fat diet group, a commonly available booklet and additional handouts, a registered dietician instructed participants in a diet consisting of less than 30% of daily energy from fat, less than 10% of daily energy from saturated fat and less than 300mg of cholesterol daily. The recommended energy intake was 500 to 1000 kcal less than the participant's calculated energy intake for weight maintenance (body weight in pounds X 10)</p>

APPENDIX A 15: Data Collection Sheets – Yancy et al. (2004)

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What was measured and how was it measured?	<p>Body weight, body composition, fasting serum lipid levels, and tolerability of diet.</p> <p>Primary Outcome Measure: Body weight and BMI</p> <p>Secondary Outcome Measures: Adherence, Diet Composition, Ketonuria, Body Composition, Vital Signs- BP and pulse rate, serum lipids and lipoproteins, other metabolic effects- serum tests for sodium, potassium, chloride, urea nitrogen, creatinine, calcium, phosphorus, total protein, albumin, uric acid.</p>
Were baseline measures used?	<p>Yes. Baseline characteristics collected were age, sex, ethnic group, mean body weight \pm SD in kg; mean BMI \pm SD in kg/m²; total cholesterol; triglycerides; LDL cholesterol; HDL cholesterol, ratio of total cholesterol to HDL and ratio of triglycerides to HDL cholesterol.</p>
Were process measures used?	<p>Diet Composition - All participants completed a 24-hour recall of food intake at baseline and take-home food records (5 consecutive days, including a weekend) that were collected at each meeting during the study. A sample of participants (13 in the low-carbohydrate diet group and 7 in the low-fat diet group) who completed the study were selected for food record analysis by the research staff on the basis of adequacy of detail in their records. A registered dietitian analyzed the food records by using a nutrition software program (Nutritionist Five, version 1.6 [First DataBank, Inc., San Bruno, California]).</p> <p>Ketonuria- Restriction of dietary intake of carbohydrates to less than 40 g/d typically results in ketonuria that is detectable by dipstick analysis, which can be used to monitor adherence to the low-carbohydrate diet (14, 15). At each return visit, participants provided a fresh urine specimen for analysis. The following semi-quantitative scale was used to categorize ketone content: none, trace (up to 0.9 mmol/L [5 mg/dL]), small (0.9 to 6.9 mmol/L [5 to 40 mg/dL]), moderate (6.9 to 13.8 mmol/L [40 to 80 mg/dL]), large80 (13.8 to 27.5 mmol/L [80 to 160 mg/dL]), and large160 (>27.5 mmol/L [>160 mg/dL]).</p> <p>Body Composition - Body composition was estimated by using bioelectric impedance (model TBF-300A [Tanita Corp., Arlington Heights, Illinois]) at approximately the same time of day (afternoon or evening) at each return visit. In a subset of 33 participants, the percentage of body fat as measured by bioelectric impedance had excellent correlation with the percentage as measured by dual-energy x-ray absorptiometry ($r = 0.93$ [95% CI, 0.87 to 0.97]).</p> <p>Blood pressure and pulse rate were measured in the non-dominant arm by using an automated digital cuff (model HEM-725C [Omron Corp., Vernon Hills, Illinois]) after the participant had been sitting for 3 minutes.</p> <p>Serum Lipids and Lipoproteins- Serum specimens for lipid measurement were obtained in the morning after at least 8 hours of fasting at the screening visit and at 8, 16, and 24 weeks.</p>

APPENDIX A 15: Data Collection Sheets – Yancy et al. (2004)

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Were process measures used? – contd.	<p>Other Metabolic Effects Serum tests for sodium, potassium, chloride, urea nitrogen, creatinine, calcium, phosphorus, total protein, albumin, uric acid, total bilirubin, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, thyroid stimulating hormone, iron, hemoglobin, leukocyte count, and platelet count were obtained at the screening visit and at 8, 16, and 24 weeks.</p> <p>The glomerular filtration rate was estimated by using an equation that included age; sex; race; and serum levels of albumin, creatinine, and urea nitrogen (Modification of Diet in Renal Disease Study equation) (16).</p> <p>Adverse Effects At all return visits, participants completed an open ended questionnaire on side effects. At the 20- and 24- week visits, participants completed a checklist of the side effects that were most often mentioned during the study.</p> <p>Statistical Analysis Analyses were performed by using S-PLUS software, version 6.1 (Insightful Corp., Seattle, Washington), or SAS software, version 8.02 In most body weight and body composition models, time and group assignment were included as fixed effects with linear and quadratic time-by-group interaction terms.</p> <p>In the fat-free mass, total body water, and vital sign models, the time-by-group interaction was treated as a categorical variable. In all body weight and body composition models, random effects included intercept and linear slope terms. For the serum outcome measure models, the time-by- group interaction was treated as a categorical variable, and an unstructured covariance was used to account for within-patient correlation over time.</p> <p>All available data, including those from participants who subsequently discontinued the study, were used for the longitudinal analyses. Mixed-effects models assume non-informative dropout, meaning that the probability of dropout may depend on covariates or a participant's previous responses but not on current or future responses (17). A <i>P</i> value of 0.05 or less was considered statistically significant.</p>
Were outcome measures identified? Are there clear validated outcomes?	<p>Primary Outcome Measure: Body Weight. BMI calculated as body weight in kg divided by height in m2.</p> <p>Secondary Outcome Measure: Adherence to the diet measured by self – report, food records and for the low CHO group, urinary ketone assessment</p>
Are the methods quantitative or qualitative?	Both.

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Safety Results	<p>Minor adverse effects were more frequent in the low CHO group.</p> <p>Adverse effects in the low-CHO vs. the low-fat group. Constipation 68% vs. 35% (P<0.001); headache 60% vs. 40% (P=0.03); halitosis (38% vs. 8%, P<0.001), muscle cramps (35% vs. 7% (P<0.001), diarrhoea 23% vs. 7%, (P=0.02); general weakness 25% vs. 8% (P=0.01) and rash 13% vs. 0% (P=0.006). One 53 year old man in the low CHO group with a family history of early heart disease was diagnosed with CHD. During this study he lost 16 kg, his serum LDL had decreased by 0.75 mmol/L (29 mg/dL) and HDL increased by 0.21 mmol/L (8mg/dL).</p>
Are there end points other than those reported that might be relevant and important	Renal function and bone health maybe relevant due to ketogenic arm of study. Apo lipoprotein a and b.
Are the endpoints relevant to actual practice	Yes and consistent with other studies
Dietary Intake and Adherence Results	<p>Diet composition measured on the basis of food records collected at each visit from a subsample of participants (13 from the Low CHO group and 7 from the low-fat group. The Low-CHO group consumed a mean (\pm SD) of 29.5 \pm 11.1g of CHO (8% of daily energy intake), 97.9\pm 24.3 of protein (26% of daily energy intake), and 110.6 \pm 27.3 g of fat (68% of daily intake) daily. The low-fat group consumed 197.6 \pm 34.2 of CHO (52% of daily energy intake), 70.5\pm 9.7g of protein (19% of daily energy intake) and 48.9 \pm12g of fat (29% of daily intake). Estimated daily energy intake was 1461.0\pm325.7 kcal in the Low-CHO group and 1502.0 \pm 162.1 kcal in the low fat group.</p>
Weight loss and cardio-protective mechanisms identified,	<p>Weight loss resulted predominantly from reduced energy intake in both groups. The method of reducing energy intake differed greatly. The low-fat diet group received counseling to restrict intake of fat, cholesterol, and energy, whereas the low-carbohydrate diet group received counseling to restrict intake of carbohydrates but not energy. The voluntary reduction in energy intake among recipients of the low-carbohydrate diet merits future research. These participants may have restricted intake because of limited food choices, or the low-carbohydrate diet may have appetite suppressant properties (21, 22).</p> <p>Other possible explanations for the discrepancy in weight loss between groups include loss of energy through ketonuria and the increased thermic effect of a high-protein diet (23). With regard to the composition of weight loss, both groups lost predominantly fat mass over 24 weeks, and the percentage of total weight loss that was fat was similar in both groups. The low-carbohydrate group lost a greater amount of water in the first 2 weeks than did the low-fat diet group; this finding confirms anecdotal reports of diuresis with the low-carbohydrate diet.</p>

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Weight Loss / Body Composition results	<p>61% (n=36) of the low-CHO group and 23% (n=14) of the low fat group lost greater than 10% of their initial body weight. (P<0.001). Over 24 weeks, participants in each group lost more fat mass than fat-free mass.</p> <p>Percentage of total weight loss that was fat loss was similar in the two groups (78% in the low-CHO group and 74% in the low-fat group)</p> <p>The low-CHO group lost a greater amount of total body water in the first two weeks than the low-fat group.</p>
Ketonuria Results	<p>Of the low-CHO Group 86% (47 of 55) had urinary ketones of as trace or greater at 2 weeks and 42% (19 of 45) at 24 weeks. Proportion with urinary ketones as moderate or greater was 64% (35 of 55) at 2 weeks and decreased to 18% (8 of 45) at 24 weeks</p>
Cardiac Risk Factor Results	<p>Vital Signs - Over 24 weeks systolic BP in the low CHO group decreased by 9.6mm Hg, diastolic BP decreased by 6.0mm Hg. In the low-fat group, systolic BP decreased by 7.5mm Hg and diastolic BP decreased by 5.2mm Hg The low CHO group had statistically greater changes in the triglyceride level, HDL cholesterol level and ratio of triglycerides to HDL Cholesterol (P=0.004, P<0.001 and P=0.02)respectively. LDL Cholesterol increased by more than 10% in 13 (30%) of 44 recipients of the low-CHO group and 5 (16%) of 31 recipients of the low-fat diet ((P>0.2)</p> <p>Perhaps the biggest concern about the low-carbohydrate diet is that the increase in fat intake will have detrimental effects on serum lipid levels (24). We found that the LDL cholesterol level did not change on average but did increase by more than 10% from baseline to week 24 in 30% of recipients of the low-carbohydrate diet who completed the study.</p>
Hormonal and Endocrine Results	Serum glucose, insulin levels and insulin sensitivity were not measured.
Exercise and Medication use	The researchers could not distinguish the effects of the nutritional supplements given only to the low CHO group. Could be a confounding factor. Supplements may have acted as an incentive for participants but may also have increased weight loss in participants.
What effect may bias have on the result?	Simulating the practice of the study sponsor- Atkins Foundation, the administration of nutritional supplements to the Low-CHO group, potentially creates a bias in favour of this group and potentially confounds the results.
The Author's conclusions - are these justified?	Compared with a low-fat diet, a low CHO diet had better participant retention and greater weight loss. During active weight loss serum triglycerides decreased more and HDL increased more with the low CHO diet than the low fat diet.

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Generalizability- the extent to which the results might apply outside the study	Weight loss and CVD marker improvement with energy restriction may be generalized.
Discussion points	<p>Over 24 weeks the low CHO group led to greater weight loss, reduction in serum triglyceride and increase in HDL cholesterol compared with a low-fat diet. Results for weight loss and serum triglycerides similar to 4 randomized controlled trials of the low – CHO diet. Rise in HDL cholesterol occurred in 1 of the 4 studies. Magnitude of weight loss comparable with that achieved by use of orlistat (9% at 6 months) and sibutramine (8% at 6months).</p> <p>Weight loss in both groups resulted from reduced energy intake however the method of reduction differed – one with advice to reduce CHO not energy and the other to restrict fat, cholesterol and energy. Voluntary reduction of energy reduction by the low-CHO group merits future research.</p> <p>Restricted intake explanations include limited food choices or the low CHO diet may have appetite suppressant properties. Loss of energy through ketonuria and increased thermic effect of a high protein diet.</p> <p>A study in which food is controlled will better determine what factors contribute to weight loss from a low-CHO diet.</p> <p>Both groups lost fat mass over 24 weeks and the percentage of total weight loss comprising fat was similar in both groups. Whilst loss of water was greater with the low-CHO group for the first 2 weeks, after this total body water levels were similar for both groups. Changes in fat-free mass in both groups were explained by loss of water not lean tissue mass. Because the low CHO may lead to an increase in LDL cholesterol it is prudent to monitor serum lipid profiles of followers of this plan.</p> <p>Decrease in serum triglycerides observed in people with normal / moderately elevated baseline levels. For people with fat induced lipemia, the low-fat option may be the preferred option for decreasing triglycerides and preventing pancreatitis.</p> <p>HDL cholesterol increased for the low-CHO group in line with other studies that found that HDL cholesterol increases when dietary CHO is replaced by saturated, monounsaturated or polyunsaturated fat.</p> <p>With low fat diets HDL decreases during active weight loss and then increases during the weight stabilization phase when the diet is maintained. LDL cholesterol and triglycerides decrease during weight loss and then increase during stabilization phase. As participants were not followed beyond the phase of active weight loss, it was not possible to state how HDL cholesterol or other lipids may change during a weight maintenance phase.</p> <p>Research may be warranted on the effects of a low-CHO diet for patients with metabolic syndrome.</p>

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Discussion points contd.	<p>Authors express view that the underlying reason for greater drop-out rate in the low-fat group was likely to be participant dissatisfaction with weight loss as compared with their peers on the low-CHO diet.</p> <p>Symptomatic adverse effects that occur at the initiation of low-CHO diets (weakness, orthostasis, headaches, constipation and muscle cramps) are short-lived and may be reduced by copious fluid intake, consumption of allowed vegetables, bouillon and a daily multivitamin and mineral supplement.</p>
Were study limitations discussed?	<p>The researchers could not distinguish the effects of the nutritional supplements given only to the low CHO group. Could be a confounding factor.</p> <p>Supplements may have acted as an incentive for participants but may also have increased weight loss in participants. The researchers have considered a systematic review to confirm that the ingredients in the supplement used in this study were not shown to induce weight loss. The essential oil supplement with fish oil potentially reduce triglycerides and increase HDL cholesterol however the authors comment that the dose of fish oil was very low compared with doses used to treat hypertriglyceridemia but they may have contributed to the changes that occurred. Supplements may also have reduced potential adverse effects of the low-CHO diet e.g. citric acid may have helped to prevent kidney stones.</p> <p>Participants were generally healthy followed only for 24 weeks limiting the generalization of the results.</p>
Future Implications discussed	<p>Further research is needed in other groups and for longer periods to determine the safety of this dietary approach.</p> <p>The low-CHO diet has not been studied with patients with chronic illness- close medical supervision would be needed. The low-CHO diet has not been studied with patients with chronic illness- close medical supervision would be needed. Weight loss may be difficult to maintain after 24 weeks</p>

Appendix B1- Dietary Design, Protocols & Weight Management Results
(Alphabetical Order) – Extracted from Appendices A2-A15 and Summarized Further.
KEY: A=Atkins Diet; N= Non-Ketogenic low-carbohydrate diet; Z =Zone Diet;
L=Low-fat conventional diet; W=Weight Watchers; O= Ornish

Studies Selected – Key Features of Dietary Design, Protocols & Weight Management Results
<p>Dansinger et al. (2005); 1 yr ; Atkins (A) : Z (Zone) : Low-Fat (L) (Ornish) : Weight Watchers (W)</p> <p>Dansinger et al. (2005) studied four diets. The Atkins group consumed less than 20 grams (g) of carbohydrates daily increased gradually to 50 g. The Zone diet group restricted carbohydrate to 40% of daily energy intake.</p> <p>The Weight Watchers Group restricted calories to 1200-1600 kcal.</p> <p>The Ornish diet group restricted fat intake to 10% of energy intake with higher levels of carbohydrate intake.</p> <p>The study noted that the mean caloric reduction from baseline were 138 kcal for Atkins, 251 kcal for Zone, 244 for Weight watchers and 192 for Ornish groups and all the diets resulted in modest weight loss at one year that was statistically significant with no statistically significant differences between the diets (P=0.4).</p> <p>The weight loss at one year was 2.1±4.8 kg (2.1%) for the Atkins group (21 (53%) of 40 completed participants), 3.2± 6.0 kg for 26 of 40 participants who completed the Zone diet, 3.0 ± 4.9 kg (3.4%) for 26 of the 40 participants who completed the Weight Watchers diet plan; and 3.3 ± 7.3 kg (3.2%) for 20 of 40 participants who undertook the Ornish diet.</p> <p>Dansinger et al. (2005) noted that there were poor sustainability and adherence rates for all the diets and that adherence level rather than diet type was the key determinant of clinical benefits.</p> <p>The theory generated from this paper is that adherence may be increased if participants can freely choose their dietary approach. Additionally, more research is needed to identify practical techniques to increase adherence and match individual preferences, lifestyle and medical conditions.</p>
<p>Foster et al. (2003); 3m, 6m &12m; A : L</p> <p>Foster et al. (2003) compared a low-carbohydrate Atkins diet with a conventional low- fat higher carbohydrate diet over three, six and twelve months and purported to be the first randomized controlled study that tested the Atkins diet.</p> <p>The Atkins diet group were asked to follow a copy Dr Atkins New Diet Revolution whilst the low fat – high carbohydrate diet prescribed 1500-1800 kcal per day for women and 1800 kcal per day for men with 60% of calories from carbohydrates, 25% of calories from fat and 15% from protein.</p> <p>Baseline weight for Atkins group was 98.7± 19.5 kg and for the low-fat group was 98.3±16.4 kg. At three months, subjects on the Atkins diet lost 6.8 ± 5.0 %. (6.7 kg ± 0.5 kg) of body weight as compared with 2.7 ±3.7% (2.65 ±0.5 kg) by the low-fat /high-carbohydrate group (P=0.001).</p> <p>At six months the difference remained significant as weight loss for the Atkins group was 7 ± 6.5 % (6.9 ±6.4 kg)as compared with a weight loss of 3.2± 5.6% (3.14 ±5.5 kg) of body weight (P=0.02) for the low fat – high carbohydrate group. At twelve months the weight loss for the Atkins group was 4.4 ± 6.7 % (4.3±6.6 kg) whilst that for the low-fat group was 2.5 ± 6.3% (2.5±6.2 kg) of body weight which was not considered significant (P=0.26).</p> <p>The weight loss data is based on an analysis in which base-line values were carried forward in case of missing data. If an alternative analysis is used that included data on</p> <p>Subjects who completed the study and data obtained at the time of the last follow-up visit for those who did not complete the study the percentage change in weight is higher (-8.1 ±4.4% for the Low-Carbohydrate (LC) group vs. -3.8±3.9% for the LF group at 3m (P=0.002); -9.7±5.7% vs. -5.3±6.4% at 6m (P=0.03) and -7.3 ±7.3 % vs. -4.5± 7.9% at 12m (P=0.27).</p> <p>This study shows that that over the short to medium term of three to six months, a low-carbohydrate Atkins type approach is likely to result in a significantly greater weight loss than a conventional low-fat approach. The low- carbohydrate group was able to achieve greater weight</p>

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<p>Foster et al. (2003); 3m, 6m &12m; A : L contd.</p> <p>loss despite unrestricted intake of protein and fat or a caloric restriction as compared with the reduced calorie, low-fat conventional dietary approach with calorie restriction to 1500-1800 calories.</p> <p>It was noted that ketosis was not a likely explanation for the increased weight loss with the low carbohydrate diet as ketones were not present for most subjects after the first six months. However the reduced energy intake with the Atkins type diet may be linked to the simplicity or monotony of the food plans or other aspects of the diet that affect appetite and dietary adherence.</p>
<p>Frisch et al. (2009); 6m & 1yr; Z : L</p> <p>Frisch et al. (2009) compared a low carbohydrate Zone type diet with a low fat conventional diet.</p> <p>The target macronutrient composition in the low carbohydrate group was less than 40% of total energy intake from carbohydrates, more than 35% energy from fat, and 25% energy from protein. The target macronutrient composition in the low fat group was more than 55% energy from carbohydrates, less than 30% energy from fat, and 15% energy from protein.</p> <p>All participants were advised to reduce their daily energy intake by at least 500 kcal. During the first six months energy intake decreased by approximately 400 kcal/d compared to baseline in both groups. At month 12, the mean energy intake had slightly increased again in both groups but remained below baseline values.</p> <p>During the study period, the low carbohydrate group had a 2-3% higher protein intake, a 4-8% higher fat intake and a 7-11% higher carbohydrate intake than the low fat group.</p> <p>At month 6, both diets resulted in similar weight loss. Weight loss was 7.2 ± 5.4 kg in the low carbohydrate group and 6.2 ± 4.8 kg in the low fat group.</p> <p>In the second half-year, mean weight regain was 1.6 kg in the low carbohydrate group and 1.9 kg in low fat group. Thus, at the end of the study at month 12, the weight loss was 5.8 ± 6.1 kg in the low carbohydrate group and 4.3 ± 5.1 kg in the low fat group, the difference considered borderline significance ($p = 0.065$).</p> <p>Furthermore, in both groups, approximately 76% of weight reduction was due to a loss of fat mass (Frisch et al. 2009).</p>
<p>Johnston et al. 2006 , 6weeks, Atkins Diet (A) : Zone Diet (Z)</p> <p>Johnston et al. (2006) compared two low-carbohydrate diets over six weeks, one of which was a ketogenic Atkins type diet while the other was a low-carbohydrate non-ketogenic diet.</p> <p>The diets aimed to be isocaloric restricting daily caloric intake to 1500 kilocalories (kcal). In Johnston et al. (2006), the weight loss results did not differ significantly. Baseline weight was 95.8 ± 5.7 kg for the Atkins group and 99.4 ± 6.1 kg for the Zone group.</p> <p>The Atkins type group lost 6.3 ± 0.6 kg (6.6% of baseline weight) whilst the Zone type group lost 7.2 ± 0.8 kg (7.2% of baseline weight). Fat losses of 3.4 kg in the Atkins group and 5.5kg in the Zone type group also did not differ significantly between the groups by week 6 ($P=0.111$).</p>
<p>Layman et al. 16 w; (2005); Z : Z+ Exercise : L : L+ Exercise</p> <p>Layman et al. (2004) compared Zone type diets with and without the inclusion of exercise to a higher-carbohydrate conventional diet protocol with and without exercise.</p> <p>The lower-carbohydrate Zone type diet allowed protein intake of 1.6g per kilogram per day (approximately 30% of energy intake), a carbohydrate: protein ratio <1.5 and dietary fats at 30% of energy intake. The higher-carbohydrate conventional protocol allowed dietary protein at 0.8g per kilogram per day (15% of energy intake), a carbohydrate to protein ratio > 3.5 and fats at 30% of energy intake.</p>

Layman et al. 16 w; (2005); Z : Z+ Exercise : L : L+ Exercise contd.

The study and menus were designed to provide the diet groups with 1700kcal per day but subjects were free-living and determined their own daily intake. The actual caloric intake was 1300-1400 kcal for the groups representing approximately 33 % energy reduction from baseline.

Actual protein intake in the lower-carbohydrate group was 107g/day (30% of energy intake) with carbohydrate: protein ratio of 1.24 (~30% of energy) and fat intake of 32% of energy.

The high carbohydrate group's intake of carbohydrates was 198g/d (61%), protein intake was 57g/d (18%) and reduced fat intake to 37g/day (25.5% of energy intake).

Exercise in the control groups averaged <100min per week against the recommendation of 30 minutes of walking 5 days a week. The Exercise groups were also recommended 30 minutes of walking 5 days a week plus 30 minutes of resistance training and stretching 2 days/week. The higher exercise group's compliance was supervised and averaged more than 200 minutes per week.

Baseline weight in the Zone group was 91.1 ± 5.1 kg and 86.1± 4.6 kg for the Zone + exercise group and 93.7 ± 3.5 kg for the LC group and 79.8 ± 2.7 kg for the LC + exercise group.

The low-carbohydrate diets achieved an average weight loss of 9.3 ± 0.8 kg after sixteen weeks while the conventional diet subjects had a lower average weight loss of 7.3 ± 0.5 kg (P<0.05). The low-carbohydrate group with exercise achieved the largest relative weight loss at 11.2%, the lower-carbohydrate control group with less exercise had 9.5%, and the higher-carbohydrate group with exercise had weight loss 8.4% whilst the higher-carbohydrate control group with less exercise achieved weight loss of 8.3%.

Subjects in the lower-carbohydrate groups together reduced fat mass by 7.3± 0.8 kg whilst the higher-carbohydrate groups had average fat mass reduction of 5.3±0.3 kg. Taking the two higher exercise groups together the average reduction in fat mass was 7.2±0.7kg whereas the non-supervised lower exercise groups reduced body fat by 5.5±0.5 kg (P<0.05).

Higher protein intake, lower carbohydrate intake and supervised exercise produced a 21.4% reduction in absolute body fat whilst the higher carbohydrate group without supervised exercise had a 12.8% reduction in body fat. A similar pattern was evident for changes in abdominal or trunk fat.

This study highlights the additive effects of the low carbohydrate-high protein diet and exercise on body composition with significant main effects of diet (P<0.01) and Exercise (P<0.001). This study reiterates the importance of caloric restriction by 20-30% per day for weight loss and that both weight loss and fat loss can be enhanced by consuming higher protein (1.6g per kilogram of body weight per day ; reduced carbohydrate and the inclusion of exercise (both cardiovascular and resistance).

Luscombe-Marsh et al. (2005); 12 w energy restriction & 4 w energy balance ; N: N

Luscombe-Marsh et al. (2005) considered two diets over sixteen weeks that restricted to carbohydrates to 30% of energy or approximately 110 grams (g) per day with variations in levels of fat and protein intake.

For the purposes of this review these diets were classified as low-carbohydrate non-ketogenic though the macronutrient composition resembles the Zone type composition more than the Atkins except after about two months of the Atkins programme when carbohydrate levels may be raised to 120g per day.

The diets undertaken implied calorie restriction to 1500kcal per day. Saturated fat was restricted to 10% of energy and fibre for both diets was 21 and 27 grams per day respectively. After twelve weeks of energy restriction there were no significant differences in weight loss, fat loss and lean mass loss between the diets.

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<p>Luscombe-Marsh et al. (2005); 12 w energy restriction & 4 w energy balance ; N: N</p> <p>Weight loss after 16 weeks was 9.7 ± 1.1 kg (10.2%) for the LF-HP (40% Protein, 30% Fat) group and 10.2 ± 1.4 kg (10.3%) in the HF-SP (20% Protein, 50% fat) group ($P=0.78$).</p> <p>Baseline weight for the LF-HP group was 94.86 kg and for the HF-SP group was 99.36 kg. From week 0 to week 16, the reduction in fat mass was $13.9 \pm 1.5\%$ and the decrease in abdominal fat mass was $17 \pm 2\%$, ($P<0.001$).</p> <p>Lean mass was reduced by $6.0 \pm 0.6\%$ ($P<0.001$). Effects of energy restriction may be confounded as weight loss and fat loss data provided after 16 weeks not 12 weeks.</p>
<p>McAuley et al. (2004), 8weeks weight loss, 8 w supervised maintenance , 8 w unsupervised maintenance, A v Z v Low-fat (L)</p> <p>McAuley et al. (2004) included in their study, two low-carbohydrate diets following the Atkins approach and the Zone diet approach and one low-fat/high-carbohydrate diet. All three diets produced weight loss expected to reduce the risk of type 2 diabetes (T2D) and CVD.</p> <p>Baseline weight for Atkins group was 96.0 ± 10.8 kg, for the Zone group was 93.2 ± 14.5 and for the low-fat group was 98.0 ± 15.1 kg. The weight loss range was assumed to be mean weight loss ± 0.5 as the range information was not available. The range for weight loss is assumed to be ± 0.5 kg as data to calculate the range was not available. Consequently the weight loss in the Atkins group was 6.6 kg ± 0.5 kg (6.9%) whilst the Zone group lost 5.4 ± 0.5 kg (5.8%).</p> <p>Both the Atkins and Zone groups lost more weight than the high- carbohydrate group who lost 4.3 ± 0.5kg (4.4%).</p> <p>The results from the Atkins and Zone diet approaches may be more favourable than a higher carbohydrate/ higher fibre diet though this could result from the reduction of mean daily caloric intake for the low-fat /high-carbohydrate group (439kcal/day) being less than that for the Atkins group (519 kcal/day) and the Zone group (522kcal/day).</p> <p>Mean fat mass reduction at 8 weeks in the Atkins group was 4.4kg, Zone group was 3.1kg and in the low-fat group was 3.4kg. After 8 weeks mean waist circumference had reduced by 8.3cm in the Atkins group, 7.7cm in the Zone group and 4.8cm in the low-fat group.</p> <p>Mean fat-free mass at 8 weeks reduced by 2kg in the Atkins group, 3.1kg in the Zone group and 1.8 kg in the low-fat group.</p>
<p>Meckling et al. (2004); 10w; Non-ketogenic low-fat diet (N) : L</p> <p>Meckling et al. (2004) compared a non-ketogenic low carbohydrate diet with a low-fat, high-carbohydrate conventional diet over 10 weeks.</p> <p>The low-carbohydrate diet design entailed reducing carbohydrate intake from 100g per day to 50-70 g by day 5 resulting in energy intake reduction to 1205-1605 kcal per day for women and 1406-2207 kcal per day for men.</p> <p>Subjects on the low-fat diet were instructed to achieve a similar energy deficit to the low-carbohydrate group. The average energy reduction over the ten week intervention for the low-carbohydrate group was 763kcal and that for the low- fat group was 607kcal representing 33% and 29% reduction of energy intake from baseline.</p> <p>The dietary protocols caused a substantial decrease in carbohydrate intake by approximately 228g per day for the low-carbohydrate group and an increase in carbohydrate intake by approximately 13g per day for the low-fat group.</p> <p>Similar weight loss was achieved in both diet groups. Baseline weight for the low-carbohydrate group was 91.0 ± 4.5 kg and for the low-fat group was 92.3 ± 3.0 kg. Assumed range was Mean ± 0.5 SD.</p>

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Meckling et al. (2004); 10w; Non-ketogenic low-fat diet (N) : L

Over the ten week trial period, the low-carbohydrate group decreased body weight by 7 kg (7.7%) whilst the low-fat group experienced a reduction of 6.8kg (7.4%).

Fat loss was significant in both groups. The low-carbohydrate recorded fat loss of 4.1kg whilst the low-fat group had fat loss of 5.4 kg.

Parker et al. (2002) ; 8w energy restriction & 4 week energy balance ; Z:L

Parker et al. (2002) compared a Zone type diet (28% protein, 42% carbohydrate and 28% fat) with a higher carbohydrate diet approach (16% protein, 55% carbohydrates and 26% fat.

Both diets were matched for fatty acid profile of which 8% was saturated fat and 12 % monounsaturated fatty acids and 5% polyunsaturates and aimed for an eight week restriction of calories to 1600 kcal per day for both diet plans.

Baseline weight for Zone group was 97.7±17.4 kg and 91.4±18.2 kg for the low-fat group. At 8 weeks the mean weight loss in the Zone group and the low-fat group was 4.5kg and 4.6% and 4.9% respectively (computed from data provided). The range was calculated assuming a spread of ±0.5 kg.

Overall after 12 weeks, weight loss of 5.2± 1.8 kg was achieved for both diet groups however this study showed a significant sex by diet effect as women lost more weight on the Zone type diet as compared with the higher carbohydrate diet (6.0 kg vs. 4.2kg) as well as fat mass (5.3 vs. 2.8 kg) and abdominal fat (1.3 vs. 0.7kg) whilst men lost more weight (5.8kg vs. 4.7kg) , fat mass (5.1kg vs. 3.8kg) and abdominal fat (1.7 vs. 1.4 kg) on the higher carbohydrate plan (Parker et al. 2002).

This study finds that a higher-protein Zone type diet compares well with a higher carbohydrate diet for weight loss over eight weeks of energy restriction (1600kcal) and may suit women dieters in preference to men (Parker et al. 2002). Energy restriction could not be adequately assessed as a driver for weight loss as results are combined for the energy restriction and energy balance phases.

Sacks et al. (2008); 6m & 2yrs; Z v L.

Sacks et al. (2008) studied a dose response test of carbohydrate intake ranging from 35% to 65% of energy. T

his study included two low-carbohydrate options of 35% and 45% of energy intake. These two diets were similar to Zone type low – carbohydrate diets whilst the other two diets had a low fat-higher carbohydrate design.

The participants in this study were prescribed a caloric deficit of 750kcal per day from baseline and the goal for physical activity was 90 minutes per day.

At six months the participants had lost an average of 6kg (7% of initial weight). After 12 months participants began to regain weight and by 24 months the weight loss recorded in all the four diet groups was similar. A total of 185 (23%) of the participants continued to lose weight from 6m to 2 yrs the mean additional weight loss was 3.6 ±3.5 kg for a mean total weight loss from baseline of 9.3 ±8.2 kg with no significant differences among the diet groups.

At 2 years 31-37% had lost at least 5% of initial weight, 14-15% of participants had lost at least 10% of initial weight and 2-4% had lost 20kg or more(P>0.2 for comparisons between the diets).

The average weight loss among the 80% of the participants who completed the trial was 4kg.

Furthermore 14-15% of the participants had a reduction of at least 10% of their initial weight.

Sacks et al. (2008) contd.

Most of the weight loss occurred in the first six months and changes from the baseline between the diets differed by less than 0.5kg of body weight and 0.5 cm of waist circumference.

Changes in waist circumference, satiety, hunger, satisfaction with the diet and attendance at group sessions was similar for all the diets and attendance at counselling and monitoring sessions was strongly associated with weight loss (0.2 kg per session attended) (Sacks et al. 2008).

The theory that may be generated from this study is that a reduction of 750 kcal per day may be more significant in generating weight loss than the macronutrient composition of the diet.

In addition prescribing a minimum intake of dietary fibre and a limit to the intake of saturated fat and cholesterol may support the weight loss process. Similarly this study re-iterated that recommending inclusion of foods with a low- glycaemic index may influence weight loss (Sacks et al. 2008).

Samaha et al. (2003); 6m; A v L

Samaha et al. (2003) compared a low carbohydrate Atkins type diet with a low fat diet.

Subjects on the low carbohydrate design were required to restrict carbohydrate intake to 30g per day or less with no restriction on total fat intake. Vegetables and fruits with a high ratio of fibre to carbohydrate were recommended.

Subjects on the low fat diet were recommended the guidelines of the National, Heart, Lung and Blood Institute including a caloric restriction sufficient to create a deficit of 500 kcal with 30% or less of total calories derived from fat.

Subjects on the low-carbohydrate Atkins diet reported a non-significantly greater reduction in caloric intake ($P=0.33$), a significantly greater decrease in percentage of calories from carbohydrates ($P<0.001$) and a significantly greater increase in calories from protein ($P<0.001$) and fat ($P=0.004$).

Subjects on the low carbohydrate diet lost more weight during the six month study (-5.8 ± 8.6 kg or 4.4%) as compared with the low fat group (-1.9 ± 4.2 kg or 1.4%). Weight loss of at least 10% of baseline weight occurred in 9 of 64 subjects (14%) as compared with 2 of 68 subjects on the low fat diet (3%).

White subjects lost more weight than black subjects (mean -13 ± 19 kg vs. -5 ± 12 kg ($P=0.009$) suggesting that weight loss strategy both in terms of adherence and appropriateness may have a cultural and / or genetic influences.

Furthermore the amount of weight loss had a significant effect on the degree of improvement in metabolic factors. 5% weight loss on a carbohydrate restricted diet had better metabolic results than those who lost a similar amount of weight while on a fat and calorie restricted diet.

The theory generated from this study is that statistically significant weight loss may be achieved using a low carbohydrate Atkins type diet.

The greater weight loss in the low CHO group however could result from the greater reduction in overall caloric intake resulting from such a diet rather than a direct effect of macronutrient composition.

Possible explanations for the lower caloric intake could suggest that subjects may have experienced greater satiety with liberal portions of protein and fat, the relative simplicity of the diet; improved compliance due to novelty of the diet (Samaha et al. (2003).

**Appendix B1- Dietary Design, Protocols & Weight Management Results
(Alphabetical Order) – Extracted from Appendices A2-A15 and Summarized Further.
KEY: A=Atkins Diet; N= Non-Ketogenic low-carbohydrate diet; Z =Zone Diet;
L=Low-fat conventional diet; W=Weight Watchers; O= Ornish**

Shai et al. (2008); 2yrs; A v L v Mediterranean diet (M)
<p>Shai et al. (2008) compared a low-carbohydrate Atkins type diet with no calorie restriction to low fat and Mediterranean diet plans where a caloric intake was restricted to 1500 kcal per day for women and 1800 kcal per day for men.</p> <p>The mean weight changes among the 272 participants who completed the 24 month study were – 5.5 ± 7.0 kg in the low carbohydrate Atkins group, -4.6 ± 6.0 kg in the Mediterranean diet group and -3.3 ± 4.1 kg in the low fat group ($P=0.03$) for the comparison between the low- carbohydrate and low-fat groups at 24 months).</p> <p>All the three groups had significant decreases in waist circumference but the differences among the groups were not significant (Shai et al. 2008).</p> <p>The theory emanating from these results is that weight loss and body composition over two years by following a diet restricted to 1500-1800 kcal per day can be matched and exceeded by a low-carbohydrate Atkins style diet that is not restricted for calories.</p> <p>Shai et al. (2008) show that the Mediterranean and low-carbohydrate Atkins type diets may be effective alternatives to the low-fat diet for weight loss and appear to be safe alternatives to the low-fat diet.</p> <p>Further theory emanating from Shai et al. (2008) is that for moderately obese subjects, the Atkins type low-carbohydrate and the Mediterranean diets may have beneficial metabolic effects and further reinforced the idea that weight loss dietary advice can be individualized according to personal preferences and metabolic needs.</p> <p>In Shai et al. (2008), despite the lack of caloric restriction for the low-carbohydrate diet, a similar caloric deficit was achieved in all the diet groups suggesting that a low-carbohydrate diet not restricted for calories may be optimal for subjects who prefer not to or are unable to follow a restricted calorie regimen.</p>
Stern et al. (2004); 12m; A v L
<p>Stern et al. (2004) undertook a one year follow-up study to Samaha et al. (2003) comparing a low carbohydrate Atkins diet with a low fat diet.</p> <p>Subjects on the low carbohydrate regime were instructed to restrict carbohydrate intake to 30g per day or less. There was no restriction on total fat intake. Vegetables and fruits with a high ratio of fibre to carbohydrate recommended.</p> <p>Subjects on low-fat diet were recommended the guidelines of the National, Heart, Lung and Blood Institute including caloric restriction sufficient to create a deficit of 500 calories with 30% or less of total calories derived from fat.</p> <p>Caloric intake decreased more by year 1 in the low carbohydrate group than in the low fat/low calorie group. The low carbohydrate group reduced carbohydrate by 52%, reduced fibre intake by 42 %, increased total fat intake by 31%; increased dietary cholesterol intake by 21%, reduced sodium intake by 21% relative to baseline.</p> <p>Participants on the low carbohydrate diet maintained most of their 6 month weight loss whereas those on the conventional diet continued to lose weight throughout the year.</p> <p>The final 1 year weight change was -5 ± 8.7 kg in the low CHO group and -3.1 ± 8.4 kg in the conventional diet group. The difference between the two diet groups was not significant.</p> <p>Persons on the low CHO diet who dropped out lost less weight than those who completed the study. In contrast weight loss was not significantly different for those on the conventional diet.</p> <p>The theory emanating from this study that weight loss differentials between a low-carbohydrate approach or a conventional diet evident at six months may diminish over a period of one year. In contrast to Foster et al. (2003) persons on the low CHO maintained most of their initial weight loss</p>

Stern et al. (2004); 12m; A v L

where as those on the conventional diet continued to lose weight. The difference may be due to more intensive counselling.

Persons on the low CHO diet who dropped out were less likely to lose weight whereas those on the conventional diet continued to lose weight whether or not they remained in the study. This observation together with the difference between diets in weight loss beyond six months suggests that a low CHO diet may be less sustainable than a conventional diet.

Yancy et al. (2004); 24 w; A v L

Yancy et al. (2004) compared a low-carbohydrate Atkins type diet with average daily energy intake of 1461 ± 325.7 kcal and a low-fat diet with average daily energy intake of 1502 ± 162.1 kcal over 24 weeks.

Baseline weight for the Atkins group completers was 98.1 ± 15.2 and for the low-fat group completers was 95.7 ± 18.0 . They noted that the low-carbohydrate group lost an average of 12.0 kg (12.9%) as compared with 6.5 kg (6.7%) in the low fat group.

61 % (n=36) of the low carbohydrate group and 23% (n=14) of the low fat group completed the study and lost more than 10% of their initial body weight ($P < 0.001$).

The expected mean change in fat mass was 9.4 kg in the low carbohydrate group and 4.8 kg for the low-fat group however the percentage of total weight loss that was fat mass was similar in the two groups (78% in the low carbohydrate group compared with 74% in the low fat group).

As compared with the other studies that included an Atkins type protocol in the design, the higher absolute and percentage weight loss shown in this study cannot be explained by the reported energy intake figures of 1461 ± 325.7 kcal.

The expected mean change in total body water was -2.4 kg in the low carbohydrate group and -1.8kg in the low carbohydrate group. Hence a change in total body water accounted in the main for the changes in fat-free mass with the low-carbohydrate group experiencing greater levels of water loss in the first two weeks as compared with the low-fat group.

The theory suggested by this study is that a low-carbohydrate diet causes a greater loss of body water initially. Additionally if an *ad libitum* diet is appropriate to the preferences and health state of an individual and the risks of using such a diet plan can be mitigated, the Atkins type weight loss plan may lead to significantly higher levels of weight loss and may provide a useful method of starting a weight loss programme.

Appendix B2 - Rationale for Notional Average Daily Calorie intake

Rationale for Notional Calorie intake level of 2000 kcal/day

UK DOH Estimated average requirement (EAR) are a daily calorie intake of 1940 for women and 2550 for men. Average : 2245

USDA (2010) dietary guidelines use a 2000 calorie level as a reference with the Nutrition facts panel.

For several studies data on caloric deficit achieved per day was provided. For several studies the data on calories intake was provided with no information on the calorie deficit achieved. Hence the notional average baseline calorie intake was assumed to be 2000 per day to estimate the daily caloric deficit for these interventions. The estimate aims to be prudent, hence was set at 2000 kcal/day.

Appendix C: Fat Loss and Waist Circumference Data from Studies Selected (Arranged Alphabetically) – Extracted from Appendices A2- A15 and Summarized Further

Study/ Study Arms A: Atkins; Z: Zone; L: low-fat; W: Weight Watchers; O:Ornish; M: Mediterranean; N: low-carbohydrate non ketogenic / DURATION
Dansinger et al. (2005) A:Z:W:O; 1 year
Noted that weight loss was highly associated with waist size reductions for all the diets with no significant difference between the diets ($r=0.86$; $P<0.001$).
Foster et al. (2003); A:L; 3m; 6m; 12m.
No measure of fat loss or waist circumference.
Frisch et al. (2009) Z: L; 6m & 1 year
For both groups 76% of weight loss was due to loss of fat mass and though the reduction in waist circumference did not differ significantly at six months. At 12 months, the decrease in waist circumference was more pronounced for the low-carbohydrate group.
Johnston et al. (2006) A:Z; 6 weeks
Of the weight loss of 7.2 ± 0.8 Kg and 6.3 ± 0.6 Kg for the Zone and Atkins diets, the reduction in fat mass was 5.5 Kg and 3.4 Kg respectively over the six week trial and was not significantly affected by the type of diet ($P=0.111$).
Layman et al. (2005) Z:Z+EX:L:L+EX; 16 weeks
Compared a Zone type diet with a low-fat diet with and without higher levels of exercise. Noted that weight loss was predominantly fat mass and increased fat loss was associated with a higher-protein/ lower carbohydrate diet and exercise.
Subjects in the low-fat group without increased exercise had 12.8% decrease in body fat whilst those in the Zone diet group with increased exercise had a 21.4% decrease in body fat (Layman et al. 2005).
Luscombe-Marsh et al. (2005) N:N; 12 weeks energy restriction (ER); 4 weeks energy balance (EB).
Both diets led to a reduction in total fat mass- $13.9\pm1.5\%$; decrease in abdominal fat mass was $17.1\pm2\%$ main effects of time, $P<0.001$). Difference between groups not significant.
McAuley et al. (2004) A:Z:L; 8 weeks
Greater reductions noted in waist circumference with the low-carbohydrate Atkins and Zone groups than the low-fat higher carbohydrate group.
Meckling et al. (2004) N:L; 10 weeks.
Did not measure waist circumference but found that significant losses in fat weight occurred in both groups. Additionally the decrease in lean mass was significant only in the low-carbohydrate group suggesting that a low-fat diet with sufficient protein may better preserve lean mass.
Parker et al. (2002) Z:L; 8 weeks ER 4 weeks EB
For total fat mass, men lost more on the low-fat diet (5.1 vs. 3.8 kg), whereas women lost more on the Zone type diet (5.3 vs. 2.8 kg), as reflected by a significant sex by diet interaction ($P=0.01$).
A significant sex by diet effect was also observed in the change in abdominal fat mass ($P<0.02$), such that men lost more fat on the low-fat diet (1.7 vs. 1.4 kg), whereas women lost more on the Zone type diet (1.3 vs. 0.7 kg). Total lean mass was reduced significantly with both diets (1.35 kg on the Low-fat diet and 0.52 kg on the Zone type diet) with no significant difference between them.

Appendix C: Fat Loss and Waist Circumference Data from Studies Selected (Arranged Alphabetically) – Extracted from Appendices A2- A15 and Summarized Further

Sacks et al. (2008); Z:L; 2 Year
Changes in waist circumference did not differ significantly between the low-carbohydrate zone type diets and the low-fat alternatives.
Samaha et al. (2003); A:L; 6m.
No measure of fat loss or waist circumference.
Shai et al. (2008)A:L:M; 2Year.
Noted that all the groups had significant decreases in waist circumference but the differences were not significant (P=0.33). Waist circumference in the low-carbohydrate group decreased by 3.8±5.2 cm, by 3.5± 5.1cm for the Mediterranean diet group and by 2.8±4.3cm in the low-fat group.
Stern et al. (2004);A:L; 12 months
No measure of fat loss or waist circumference.
Yancy et al. (2004) A: L; 24 weeks.
Both groups lost predominantly fat mass over 24 weeks and percentage of fat loss was similar for the two groups.

**Appendix D : Adverse Effects & Safety Results
(ARRANGED ALPHABETICALLY - EXTRACTED FROM APPENDICES A2 – A15
and Summarized Further)**

KEY: A=Atkins Diet; N= Non-Ketogenic low-carbohydrate diet; Z =Zone Diet;
L=Low-fat conventional diet; W=Weight Watchers; O= Ornish

Dansinger et al. (2005) A: Z: W: O; 1 year
<p>No evidence of clinically significant renal impairment in any diet group. This would be a concern for the low CHO groups.</p> <p>Study limited in ability to exclude long-term safety risks or occasional dangerous adverse effects resulting from diets though no short-term safety risks were found</p>
Foster et al. (2003) A:L; 3months (m) ; 6m; 12m
<p>Urinary Ketones- The % of patients who tested positive for urinary ketones was significantly greater in the low CHO group in relation to the conventional diet group but there were no significant differences after 3 months. No significant relation between weight loss and ketosis at any time during the study</p> <p>The study was focused on weight and specific risk factors for CHD. It did not evaluate effects on other important clinical end points such as renal function, bone health and exercise tolerance</p> <p>Health concern of consuming unrestricted saturated fat with potential to increase LDL cholesterol – established risk factor for coronary heart disease (CHD). At 3 months LDL cholesterol increased for low-CHO group but decreased in subjects on conventional diet group so difference significant. Over the longer term LDL levels closer to baseline values and not significantly different between groups</p>
Frisch et al. (2009) Z:L; 6m & 1 year
<p>No safety results reported</p>
Johnston et al. (2006) A:Z; 6 weeks (w)
<p>Creatinine Clearance Values- These did not exceed baseline values at week 6 but at 2 weeks for the KLC they were 20% above baseline. A higher creatinine clearance rate may be a normal physiologic response but in persons with a compromised renal function complications may occur. Hence persons at risk of kidney disease should carefully consider KLC diets.</p> <p>AA: EPA was 90% higher after week 6 on the KLC. As inflammation is associated with faster rates of kidney function loss and elevated ratios of fatty acids is associated with increased inflammation and tumourogenesis in rat models.</p> <p>Plasma uric acid and urinary calcium typically higher with high-protein diets were not significantly higher at trial week 6 than at baseline.</p>
Layman et al. (2005) Z:Z+EX:L:L+EX; 16w.
<p>No safety results discussed. Apo lipoprotein a and b as a significant risk factor for CVD disease along with HDL and triglycerides would have been relevant and important. BP was not measured or reported.</p>
Luscombe – Marsh et al. (2005) N(LF-HP): N(HF-SP); 12 weeks Energy Restriction (ER) 4 w Energy Balance (EB)
<p>Urinary calcium and sodium excretion remained unchanged from week 0 to week 16 (3.5 ± 0.4 and 4.1 ± 0.4 mmol/24 h for week 0 and week 16 calcium values, respectively, and 181 ± 31 and 158 ± 11 mmol/24 h for week 0 and week 16 sodium values), as did concentrations of the bone-turnover markers (94 ± 5.1 and 102 ± 5.2 mmol/l for week 0 and week 16 pyridinoline: creatinine values, respectively, and 26 ± 1.3 and 28 ± 1.4 nmol/ mmol for deoxypyridinoline: creatinine values)</p>

**Appendix D : Adverse Effects & Safety Results
(ARRANGED ALPHABETICALLY - EXTRACTED FROM APPENDICES A2 – A15
and Summarized Further)**

KEY: A=Atkins Diet; N= Non-Ketogenic low-carbohydrate diet; Z =Zone Diet;
L=Low-fat conventional diet; W=Weight Watchers; O= Ornish

McAuley et al. (2004) A:Z:L; 8 w
<p>Observed increases in LDL cholesterol with the Atkins high- fat diet were less than expected. The LDL levels with the Atkins diet were significantly higher in the HF Atkins group than in the HP Zone group. The HF Atkins group produced a marked increase in LDL cholesterol in a small number of participants suggesting that some individuals may be particularly sensitive to substantial increases in fat intake.</p> <p>Apo lipoprotein a and b, renal and bone health should have been studied as one arm of the study was following the HF Atkins Diet.</p>
Meckling et al. (2004) N:L; 10w
<p>There was an increase in circulating β hydroxybutyrate at the 2- and 4-wk time points in the LC group that remained numerically higher for the remainder of the study but not statistically different from the high at 2–4 wk or baseline. There were no statistical differences between the LC and LF subjects after wk 4.</p> <p>There was no change in β-hydroxybutyrate concentration over time in the LF group.</p>
Parker et al. (2002) Z:L; 8 w ER 4 w EB
<p>No side effects reported.</p> <p>Renal function and bone health review maybe relevant due to high-protein Zone arm of study. Apo lipoprotein a and b not measured.</p>
Sacks et al. (2008) Z:Z:L:L; 2 yr
<p>Adverse events were reported by 57 participants (7%); there were no significant differences in the rates among diets.</p> <p>The ratio of urinary microalbumin to creatinine was more than 30 in five participants in the average-protein group and in five participants in the high-protein group at 6 months and in seven participants, all in the average protein groups, at 2 years.</p> <p>There was a larger decrease in urinary nitrogen excretion from baseline in the average-protein group than in the high protein group (a difference in the change of 1.6 g at 6 months and 0.8 g at 2 years. These differences correspond to a difference in dietary protein of 10 g per day and 5 g per day, respectively.</p>
Samaha et al. (2003) A:L; 6m
<p>No clinically significant change in uric acid levels in either group.</p> <p>One death and hospitalisation in the low CHO group not deemed to be diet related.</p>
Shai et al. (2008) A:L:M; 2 yr
<p>The proportion of participants with detectable urinary ketones at 24 months was higher in the low-carbohydrate group (8.3%) than in the low-fat group (4.8%) or the Mediterranean-diet group (2.8%) (P = 0.04).</p>
Stern et al. (2004) A:L; 12m.
<p>Blood urea nitrogen levels increased more in the low CHO group but changes in uric acid levels were not clinically significant.</p> <p>3 individuals on the low CHO group died during the study but these were not regarded as diet related.</p>

**Appendix D : Adverse Effects & Safety Results
(ARRANGED ALPHABETICALLY - EXTRACTED FROM APPENDICES A2 – A15
and Summarized Further)**

KEY: A=Atkins Diet; N= Non-Ketogenic low-carbohydrate diet; Z =Zone Diet;
L=Low-fat conventional diet; W=Weight Watchers; O= Ornish

Yancy et al. (2004) A:L; 24w.

Minor adverse effects were more frequent in the low CHO group.

Adverse effects in the low-CHO vs. the low-fat group.

Constipation 68% vs. 35% ($P<0.001$);
headache 60% vs. 40% ($P=0.03$);
halitosis (38% vs. 8%, $P<0.001$),
muscle cramps (35% vs. 7% ($P<0.001$),
diarrhoea 23% vs. 7%, ($P=0.02$);
general weakness 25% vs. 8% ($P=0.01$) and
rash 13% vs. 0% ($P=0.006$).

One 53 year old man in the low CHO group with a family history of early heart disease was diagnosed with CHD. During this study he lost 16 kg, his serum LDL had decreased by 0.75 mmol/L (29 mg/dL) and HDL increased by 0.21 mmol/L (8mg/dL).

APPENDIX E: LIPID CONTROL RESULTS
(EXTRACTED FROM APPENDICES A2 - A15 - ARRANGED ALPHABETICALLY)
KEY: A=Atkins Diet; N= Non-Ketogenic low-carbohydrate diet; Z =Zone Diet;
L=Low-fat conventional diet; W=Weight Watchers; O= Ornish

Study/Study Arms	Lipid Control Results
Dansinger 2005- 1 yr A:Z:W:O	<p>All diets reduced mean LDL cholesterol levels at 1 year though for the Atkins Group the reduction was not statistically significant (P=0.07).</p> <p>All diets significantly increased mean HDL cholesterol except for Ornish Group (P=0.6). The LDL/HDL ratio decreased approximately 10% for each group (P<0.05).</p> <p>No diet programme significantly altered triglycerides at 1 year.</p>
Foster 2003- 3m,6m,12m A:L	<p>No significant differences between the groups in the total or LDL cholesterol concentration except at month 3 when values were lower in the conventional diet group.</p> <p>The relative increase in HDL cholesterol and relative decrease in triglyceride concentrations was greater in the group on the low CHO diet than in the conventional diet throughout the study.</p>
Frisch 2009- 6m & 1 yr Z:L	<p>Triglyceride levels did not change from baseline to month 6 and month 12 in the low-fat (DGE) group, but declined in the Zone type (LOGI) group by 14% at month 6, and 7% at month 12 compared to baseline values.</p> <p>HDL-cholesterol decreased in the DGE group until month 6, but rose again in the second half year, whereas this parameter remained unchanged in the LOGI group.</p> <p>Changes from baseline in triglyceride and HDL-cholesterol levels differed significantly between the LOGI and DGE groups at month 6. However, these differences disappeared later on in the study.</p> <p>Total-cholesterol was not affected in the LOGI-group but increased in the DGE group between month 6 and 12. Nevertheless, total cholesterol did not differ significantly between groups at any time point.</p>
Johnston 2006 – 6 w A:Z	<p>Compared with baseline, the 6 week LDL concentrations increased for 5 Atkins dieters and decreased in the remaining 4 Atkins dieters. In comparison LDL cholesterol was raised in 2 Zone type dieters and decreased in the remaining 8 Zone type dieters.</p> <p>HDL cholesterol concentrations fell 9% during the 6 week trial in both diet groups.</p>
Layman 2005-16w Z:Z+EX:L:L+EX	<p>Initial serum lipid concentrations did not differ among all groups. After 16 wk of weight loss, changes in TC, LDL were greater in the Low-fat (CHO) and the low-fat +EX (CHO+EX) than in the Zone (PRO) Groups</p> <p>Serum TC in the CHO and CHO+EX groups decreased by 0.51 ± 0.09 mmol/L (9.2%) and LDL-C decreased by 0.38 ± 0.08 mmol/L (10.4%) from baseline values. In the Zone (PRO) and PRO+EX groups these decreased by 0.21 ± 0.12 mmol/L (3.7%) and 0.08 ± 0.11 mmol/L (1.7%). Changes in TAG were highest in the PRO groups by 0.32 ± 0.06 mmol/L (20.2%). In the CHO and CHO+EX groups TAG concentration decreased by 0.1 ± 0.07 mmol/L (5.2%).</p> <p>HDL-C concentrations changed in opposite directions for the 2 diet treatments. The PRO groups had a net increase of 0.01 ± 0.03 mmol/L in HDL-C and the CHO groups decreased by 0.08 ± 0.03 mmol/L. Ratios of TAG/HDL were more responsive to the PRO diet than the CHO diet No significant effects of EX were apparent for any lipid outcomes.</p>

APPENDIX E: LIPID CONTROL RESULTS
(EXTRACTED FROM APPENDICES A2 - A15 - ARRANGED ALPHABETICALLY)
KEY: A=Atkins Diet; N= Non-Ketogenic low-carbohydrate diet; Z =Zone Diet;
L=Low-fat conventional diet; W=Weight Watchers; O= Ornish

Study/Study Arms	Lipid Control Results
<p>Luscombe – Marsh (2005)- 8w ER, 4w EB</p> <p>N(LF-HP): N(HF-SP)</p>	<p>Improvements in fasting serum lipid concentrations did not differ significantly between the LF-HP and HF-SP groups, and there were no time-by-diet or time-by-diet- by-sex interactions for any of these variables.</p> <p>Total cholesterol was reduced by $6.6 \pm 1.4\%$ at week 12 compared with week 0, and it remained reduced by $2.9 \pm 1.4\%$ at week 16 (main effect of time, $P < 0.001$).</p> <p>LDL cholesterol was reduced by $3.4 \pm 1.9\%$ at week 12 and by $0.7 \pm 2.3\%$ at week 16 ($P = 0.005$).</p> <p>HDL cholesterol was increased by $6.8 \pm 2.0\%$ at week 12, and at the end of week 16 it remained $10.1 \pm 2.1\%$ above baseline ($P < 0.001$).</p> <p>The serum triacylglycerol concentration was reduced by $23.1 \pm 3.6\%$ by week 12 and by $15.9 \pm 4.3\%$ at week 16 (main effect of time, $P < 0.001$).</p>
<p>McAuley 2004 -8w A:Z:L</p>	<p>When compared with the Low-fat -HC diet, the Atkins-HF and Zone- HP diets were shown to produce significantly greater reductions in several parameters, including triglycerides (HF -0.30 mmol/l, HP -0.22 mmol/l).</p> <p>LDL cholesterol decreased in individuals on the HC and HP diets, but tended to fluctuate in those on the HF diet to the extent that overall levels were significantly lower in the HP group than in the HF group (-0.28 mmol/l, 95% CI $0.04-0.52$, $p=0.02$). Of those on the HF diet, 25% showed a $>10\%$ increase in LDL cholesterol, whereas this occurred in only 13% of subjects on the HC diet and 3% of those on the HP diet.</p> <p>Observed increases in LDL cholesterol with the Atkins high- fat diet were less than expected. The LDL levels with the Atkins diet were significantly higher in the HF Atkins group than in the HP Zone group. The HF Atkins group produced a marked increase in LDL cholesterol in a small number of participants suggesting that some individuals may be particularly sensitive to substantial increases in fat intake.</p> <p>Fasting triglycerides, although reduced by all three diets, fell to a significantly greater extent with the HP and HF diets than with the HC diet.</p> <p>In accordance with a previous Study (Foster et al. 2003), the HF Atkins diet produced a small increase in HDL cholesterol which was similar to that observed for the HP Zone diet, but greater than that produced by the HC conventional diet.</p> <p>Overall, LDL cholesterol was lower in the HP group than in the HC group. Levels of LDL cholesterol were increased by $>10\%$ in eight individuals (25%) in the HF Atkins group, four (13%) in the HC group and one (3%) in the HP Zone group.</p>
<p>Meckling 2004 -10w N :L</p>	<p>Total cholesterol values at baseline indicated that six subjects in each diet category had hypercholesterolemia (>6.2 mm) and six more had borderline hypercholesterolemia ($5.2-6.2$ mm). After 10 wk, significant improvements in total cholesterol values were only observed in the LF group. Group results indicated that total and LDL cholesterol levels were unchanged from baseline in LC subjects, whereas total cholesterol decreased by 1.6 mm. LDL cholesterol decreased by 1.3 mm in LF subjects. LF subjects also showed a significant decrease (-0.3 mm) in HDL cholesterol. LC subjects showed a significant increase ($+0.14$) in HDL cholesterol. Group results indicated that both LC and LF groups saw a decrease of 0.4 mm in total triglyceride values over the intervention period</p>

APPENDIX E: LIPID CONTROL RESULTS

(EXTRACTED FROM APPENDICES A2 - A15 - ARRANGED ALPHABETICALLY)

KEY: A=Atkins Diet; N= Non-Ketogenic low-carbohydrate diet; Z =Zone Diet;
L=Low-fat conventional diet; W=Weight Watchers; O= Ornish

Study/Study Arms	Lipid Control Results
Parker 2002-8w ER; 4w EB Z (HP):L(LP)	<p>LDL cholesterol reduction was significantly greater on the HP diet (5.7%) than on the LP diet (2.7%) ($P<0.01$).</p> <p>Total cholesterol concentrations decreased more on the HP diet than on the LP diet, as reflected by a diet by time interaction of $P= 0.009$.</p> <p>For all subjects, triacylglycerol concentrations decreased at week 12 ($P<0.001$), and there was no diet or sex effect.</p> <p>There was no effect of time or diet for HDL cholesterol concentrations.</p>
Sacks 2008-2 yrs Z:Z:L:L	<p>At 2 years, the two low-fat diets and the highest-carbohydrate diet decreased low-density lipoprotein cholesterol levels more than did the high-fat diets or the lowest-carbohydrate diet (low-fat vs. high-fat, 5% vs. 1% [$P = 0.001$]; highest carbohydrate vs. lowest-carbohydrate, 6% vs. 1% [$P = 0.01$]).</p> <p>The lowest-carbohydrate diet increased HDL cholesterol levels more than the highest-carbohydrate diet (9% vs. 6%, $P = 0.02$).</p> <p>There was a larger increase from baseline in the HDL cholesterol level, a biomarker for dietary carbohydrate, in the lowest-carbohydrate group than in the highest-carbohydrate group (a difference in the change of 2 mg per decilitre at 2 years). This difference corresponds to a predicted difference in carbohydrate intake of 6%.</p> <p>All the diets decreased triglyceride levels similarly, by 12 to 17%.</p>
Samaha 2003-6m A:L	<p>Greater decrease in the mean triglyceride level in the low CHO-Atkins group than in the low fat group ($-20\pm 31\%$, $P=0.001$).</p> <p>Atkins subjects had a greater decrease in triglyceride levels irrespective of whether they were on lipid lowering drugs ($-25\pm 38\%$ vs. $8\pm 35\%$ with lipid lowering drugs – $P=0.01$) and $-16\pm 46\%$ vs. $-1\pm 25\%$ without lipid lowering drugs.</p> <p>In a separate analysis of subjects who were not taking medications – 28 on the low fat diet and 24 on the low CHO diet, the mean reduction in the triglyceride level was greater in the low CHO group : $-20\pm 42\%$ vs. $2\pm 28\%$– $P=0.001$)</p> <p>Assignment to the low CHO diet ($P=0.01$) and the amount of weight lost ($P<0.001$) were each independent predictors of a decrease in the triglyceride level however this was limited to subjects who lost more than 5% of base-line weight.</p> <p>Total cholesterol, HDL and LDL did not change significantly during the six months or between groups.</p>
Shai 2008-2yrs A:L:M	<p>HDL cholesterol increased during the weight-loss and maintenance phases in all groups, with the greatest increase in the low-carbohydrate group (8.4 mg per decilitre [0.22 mmol per litre], $P<0.01$ for the interaction between diet group and time), as compared with the low-fat group (6.3 mg per decilitre [0.16 mmol per litre]).</p> <p>Triglyceride levels decreased significantly in the low-carbohydrate group (23.7 mg per decilitre [0.27 mmol per litre], $P = 0.03$ for the interaction between diet group and time), as compared with the low-fat group (2.7 mg per decilitre [0.03 mmol per litre]).</p> <p>LDL cholesterol levels did not change significantly within groups, and there were no</p>

APPENDIX E: LIPID CONTROL RESULTS**(EXTRACTED FROM APPENDICES A2 - A15 - ARRANGED ALPHABETICALLY)****KEY: A=Atkins Diet; N= Non-Ketogenic low-carbohydrate diet; Z =Zone Diet;
L=Low-fat conventional diet; W=Weight Watchers; O= Ornish**

Shai 2008- 2yrs A:L:M Contd.	<p>significant differences between the groups in the amount of change.</p> <p>Overall, the ratio of total cholesterol to HDL cholesterol decreased during both the weight-loss and the maintenance phases. The low-carbohydrate group had the greatest improvement, with a relative decrease of 20% ($P = 0.01$ for the interaction between diet group and time), as compared with a decrease of 12% in the low-fat group.</p>
Stern 2004- 12m A:L	<p>Changes in total and LDL cholesterol were not significantly different between groups.</p> <p>Triglyceride levels decreased more in the low CHO group than in the conventional diet group ($P=0.044$ before and $P=0.041$ after adjustment for baseline variables. A separate sensitivity analysis that included only the 87 persons who completed the study confirmed this finding. Assignment to the low CHO group and greater weight loss were each independent predictors of a decrease in triglyceride concentration suggesting a direct effect of the low CHO diet on triglyceride reduction.</p> <p>The HDL cholesterol concentration decreased more in the conventional diet group than in the low-CHO group ($P=0.025$ before and $P=0.014$ after adjusting for baseline variables. The results indicated a direct diet-related effect on HDL cholesterol.</p>
Yancy 2004 – 24w A:L	<p>The low CHO group had statistically greater changes in the triglyceride level, HDL cholesterol level and ratio of triglycerides to HDL Cholesterol ($P=0.004$, $P<0.001$ and $P=0.02$) respectively. LDL Cholesterol increased by more than 10% in 13 (30%) of 44 recipients of the low-CHO group and 5 (16%) of 31 recipients of the low-fat diet ($P>0.2$)</p> <p>Perhaps the biggest concern about the low-carbohydrate diet is that the increase in fat intake will have detrimental effects on serum lipid levels (24). We found that the LDL cholesterol level did not change on average but did increase by more than 10% from baseline to week 24 in 30% of recipients of the low-carbohydrate diet who completed the study.</p>

**APPENDIX F: ENDOCRINE & HORMONAL RESULTS FOR STUDIES SELECTED
(ARRANGED ALPHABETICALLY)**

(Extracted From Appendices A2 - A15 and Summarized Further)

KEY: A=Atkins Diet; N= Non-Ketogenic low-carbohydrate diet; Z =Zone Diet;

L=Low-fat conventional diet; W=Weight Watchers; O= Ornish

	Blood Glucose, Glycosylated Hemoglobin	Insulin Resistance, Insulin sensitivity
Dansinger 2005- 1 Yr A:Z:W:O	Improvements in blood Glucose and Insulin levels noted for all four diets at 2m, 6m and 12m. The lower carbohydrate diets	The lower carbohydrate diets Atkins and Zone more likely to reduce insulin in the short term (2m) though Atkins failed to significantly reduce mean fasting insulin levels at one year.
Foster 2003- 3m,6m,12m A:L	Oral glucose-tolerance test- The area under the glucose curve did not change significantly in either group throughout the study.	The area under the insulin curve decreased in both groups, but there were no significant differences between groups. There were no significant differences between groups in insulin sensitivity (assessed by the quantitative insulin-sensitivity check index). Both groups had significant increases in insulin sensitivity at six months, but the values were not significantly different from base line at one year
Frisch 2009 6m & 1 Yr Z:L	HbA1c reduced by 0.2 % \pm 0.2 for both groups at 6m and 12m. For the low carb group Glucose reduced by -0.26 ± 0.76 mmol/l at 6 months and by 0.25 ± 0.75 at 12months and for the high carb group by -0.28 ± 0.14 at 6 m and 0.14 ± 0.46 at 12months.	No Comment
Johnston 2006 – 6w A:Z	No Comment	Insulin sensitivity was significantly improved by both LC diets
Layman 2005 – 16 w Z:Z+EX:L:L+EX	No comment	No Comment
Luscombe – Marsh (2005)- 12 w – ER 4w - EB N(LF-HP): N(HF-SP)	At week 16, the increase in plasma glucose in response to the test meals was less than that at week 0. There was no significant effect of diet or any time-by-diet or time-by-diet-by sex interactions on plasma glucose responses.	Improvements in fasting serum insulin, the HOMA index of insulin resistance, and in fasting serum free fatty acids were also not significantly different in the LF-HP and HF-SP groups. After 16 wk, the decrease in fasting serum insulin was $25 \pm 4.2\%$ (main effect of time, $P < 0.001$) and the HOMA insulin resistance index was reduced by $34 \pm 8.8\%$ ($P < 0.001$).
McAuley 2004- 8w A:Z:L	No significant differences were observed between the dietary groups with respect to fasting and 2-h glucose and fasting insulin.	Insulin levels decreased with all three diets. This study suggests that the popular diets reduced insulin resistance to a greater extent than the standard dietary advice did.
Meckling 2004- 10w N :L	Although individual results suggested some improvements in glucose control, group results indicated that there was no significant decrease in fasting serum glucose or either LF or LC interventions. This resulted in a significant decrease in the insulin to glucose ratio for the LC group after diet intervention.	However, fasting insulin levels were significantly lower after 10 wk of the LC diet, but not the LF diet. There was no change in fasting glucose or insulin to glucose ratio for the LF subjects.

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	Blood Glucose, Glycosylated Hemoglobin	Insulin Resistance, Insulin sensitivity
Parker 2002- 8w ER, 4w EB Z:L	Glycemic control - Fasting and 1-, 2-, and 3-h plasma glucose concentrations were reduced by both dietary interventions ($P < 0.001$); however, no significant effects of diet or sex were observed. HbA1c decreased by 9.4% between baseline and week 12 ($P < 0.001$). There were no significant differences observed for diet or sex.	Fasting and 2-h insulin concentrations were reduced at weeks 8 and 12 (both $P < 0.001$). The insulin, glucose product was reduced by 42% at 3 h at week 12.
Sacks 2008- 2 Yr Z:Z:L:L	All the diets except the one with the highest carbohydrate content decreased fasting serum insulin levels by 6 to 12%; the decrease was larger with the high-protein diet than with the average-protein diet (10% vs. 4%, $P = 0.07$).	The metabolic syndrome was present in 32% of the participants at baseline, and the percentage was lower at 2 years, ranging from 19 to 22% in the four diet groups ($P = 0.81$ for the four-way comparison).
Samaha 2003- 6m A:L	Glycemic control: Fasting glucose decreased more in the Low CHO group than the low fat group at six month ($-9 \pm 19\%$ vs. $-2 \pm 17\%$ ($P=0.02$)) though this change was more significant for diabetic subjects with no significant change in the levels in non-diabetic subjects on either diet. Similarly diabetic subjects showed a greater decrease in glycosylated haemoglobin compared with those on low-fat diets.	By six months seven subjects in the low CHO group had dose reductions in oral hypoglycaemic or insulin as compared to 1 in the low fat group. Insulin sensitivity increased more in the low CHO subjects than on the low fat diet. Here again assignment to low CHO diet and weight loss were independent predictors of an improvement in insulin sensitivity.
Shai 2008- 2 Yr A:L:M	Among the 36 participants with diabetes, only those in the Mediterranean-diet group had a decrease in fasting plasma glucose levels (32.8 mg per deciliter); this change was significantly different from the increase in plasma glucose levels among participants with diabetes in the low-fat group ($P<0.001$ for the interaction between diet group and time). There was no significant change in plasma glucose level among the participants without diabetes ($P<0.001$ for the interaction among diabetes and Mediterranean diet and time). Among the participants with diabetes, the proportion of glycated hemoglobin at 24 months decreased by $0.4 \pm 1.3\%$ in the low-fat group, $0.5 \pm 1.1\%$ in the Mediterranean-diet group, and $0.9 \pm 0.8\%$ in the low-carbohydrate group. The changes were significant ($P<0.05$) only in the low-carbohydrate group ($P = 0.45$ for the comparison among groups).	In contrast, insulin levels decreased significantly in participants with diabetes and in those without diabetes in all diet groups, with no significant differences among groups in the amount of decrease.

**APPENDIX F: ENDOCRINE & HORMONAL RESULTS FOR STUDIES SELECTED
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KEY: A=Atkins Diet; N= Non-Ketogenic low-carbohydrate diet; Z =Zone Diet;

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	Blood Glucose, Glycosylated Hemoglobin	Insulin Resistance, Insulin sensitivity
Stern 2004-12m A:L	Glycosylated haemoglobin in the small group with diabetes (n=54) decreased more in the low-CHO group after adjusting for baseline differences. The results show a direct effect of the low CHO diet on glycemic control	Insulin Sensitivity: The difference between the 2 diet groups was not significant.
Yancy 2004-24w A:L	Not Measured	Not measured

Appendix G: Hypertension Results for Selected Studies.

(ARRANGED ALPHABETICALLY – Extracted from Appendices A2 –A15 and Summarized Further)

KEY: A=Atkins Diet; N= Non-Ketogenic low-carbohydrate diet; Z =Zone Diet;

L=Low-fat conventional diet; W=Weight Watchers; O= Ornish

Dansinger et al. (2005) A: Z: W: O; 1 Year
The lower CHO diets (Atkins and Zone) reduced diastolic BP in the short term.
Foster et al. (2003) A:L; 6m; 12m
Systolic BP did not change significantly in either group. Diastolic BP decreased in both groups but there were no significant differences between the groups.
Frisch et al. (2009) Z:L; 6m , 1 Yr
Diastolic blood pressure decreased in both groups, whereas systolic blood pressure was significantly higher at month 12 in the low-fat group compared with the low-carbohydrate group. The differences in systolic blood pressure at month 12 remained significant after adjustments were made for fat free mass and sex distribution.
Johnston et al. (2006) A:Z; 6w Layman et al. (2005) Z:Z+EX:L:L+EX 16w
BP was not measured or reported.
Luscombe – Marsh et al. (2005) N(LF-HP): N(HF-SP) 12 w ER; 8w EB
Systolic blood pressure decreased from 130±1.89 mm Hg at week 0 to 123±1.5 mm Hg at week 16 (main effect of time, $P<0.001$), but diastolic blood pressure remained unchanged (72 ± 1.3 mm Hg at week 0 and 71 ± 1.0 mm Hg at week 16).
McAuley et al. (2004) A:Z:L;8w
Systolic and diastolic blood pressures were modestly reduced. Diastolic blood pressure was significantly lower in the Atkins group than in the Low-fat group (–3 mm Hg, 95% CI –6 to 0, $p=0.03$). No significant differences were observed between the dietary groups with respect to systolic blood pressure.
Meckling et al. (2004) N :L; 10w
Twelve of 31 subjects completing all 10 wks of the study had some form of abnormal blood pressure at baseline. The group results indicated that both diets were equally effective in reducing systolic blood pressure by about 10 mm Hg and diastolic blood pressure by 5 mm Hg.
Parker et al. (2002) Z:L; 8w ER, 4 w EB
Systolic blood pressure fell significantly by 8 mmHg and diastolic blood pressure by 4 mmHg at week 8 ($P < 0.001$) with no differential effect of diet. During the weight stabilization period between weeks 8 and 12, systolic blood pressure rose by 3 mmHg and diastolic blood pressure by 1 mmHg ($P < 0.001$). This was also not affected by diet composition.
Sacks et al. (2008) Z:Z:L:L; 2 Yr
Blood pressure decreased from baseline by 1 to 2 mm Hg, with no significant differences among the groups ($P>0.59$ for all comparisons).
Samaha et al. (2003) A:L; 6m
BP: Systolic and diastolic BP decreased by 2mm Hg and 1mm Hg respectively in the low CHO group. In the low fat group both measures decreased by 2mm Hg but there was no significant difference between the groups.
Shai et al. (2008) A:L:M; 2 Yr
Systolic blood pressure fell by 4.3±11.8 mm Hg in the low-fat group, 5.5±14.3 mm Hg in the Mediterranean-diet group, and 3.9±12.8 mm Hg in the low-carbohydrate group ($P = 0.64$ for the comparison among groups). The corresponding decreases in diastolic pressure were 0.9±8.1, 2.2±9.5, and 0.8±8.7 mm Hg ($P = 0.43$ for the comparison among groups).
Stern et al. (2004) A:L; 12m
Systolic and diastolic BP increased from baseline by 2±15 mm Hg and 1±10mm Hg for the conventional diet group and 1±19 and 3±15 for the low-carbohydrate group respectively. The differences between the groups were not significant.
Yancy et al. (2004) A:L; 24 w
Over 24 weeks systolic BP in the low-carbohydrate group decreased by 9.6mm Hg, diastolic BP decreased by 6.0 mm Hg. In the low-fat group, systolic BP decreased by 7.5mm Hg and diastolic BP decreased by 5.2 mm Hg.